STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 198626

TO: YEVGENY VALENROD
Location: REM/5D18/5C18
Art Unit: 1621
August 15, 2006

Case Serial Number: 10/600132

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

Paul A

Rush Search Agmt

8-704

ACCESS DB # 188626

PLEASE PRINT CLEARLY

FOR OFFICE USE ONLY

T K Page

SPE, AU 1621

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Yevgeny Valpenrod Examiner #: 82310 Date: 08/14/06

Art Unit: 1621 Phone Number: 2-9049 Serial Number: 10/600,132

Location (Bldg/Room#): 5D18 (Mailbox #): 5C18 Results Format Preferred (circle): (PAPER) DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Polymorphs of suberoylanilide hydroxamic acid

Inventors (please provide full names): Thomas Miller; Victoria Richon

Earliest Priority Date: 03/04/02

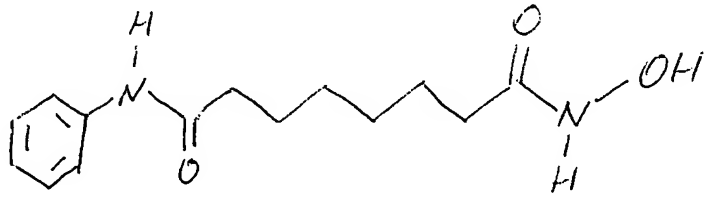
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

claims 1-39 are being examined

Search: SAHA (suberoylanilide hydroxamic acid)



L5
L6
L8
L9
L12

terms: dry "and" id .no hids other than the inventors, thus dry "or"

- X-ray diffraction (of SAHA) L9
- Differential scanning Calorimetry (DSC) L10
- alcohol solvent (particularly methanol & ethanol & iso-propanol)
- gelatin (don't do this term alone only in combination with solvent or delivery or dosage)
- delivery & intravenous

```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:03:04 ON 18 AUG 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 18 Aug 2006  VOL 145 ISS 9
FILE LAST UPDATED: 17 Aug 2006  (20060817/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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=>

=> d stat que l26
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L2               STR
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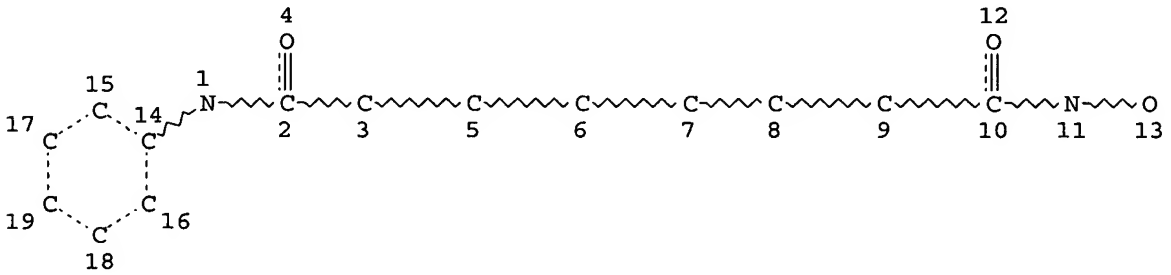


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
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L5           180 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 NOT L1
L6               SEL  PLU=ON  L1 1- CHEM :        4 TERMS
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L20           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L9
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L26  ANSWER 1 OF 44  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:149498  HCAPLUS
DOCUMENT NUMBER:          144:213019
TITLE:                    Preparation of amino hydroxamic acid urea derivatives
                          as histone deacetylase inhibitors
INVENTOR(S):              Belvedere, Sandro; Hamblett, Christopher Laurence;
                          Miller, Thomas A.; Witter, David J.; Yan, Jiaming
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA; Aton Pharma, Inc.
SOURCE:                   PCT Int. Appl., 71 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     --------------       ----   --------    --------------------    --------
     WO 2006017216         A1    20060216    WO 2005-US24514         20050708
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        US 2004-587186P     P  20040712
OTHER SOURCE(S):          MARPAT 144:213019
AB   The invention relates to hydroxamic acid derivs.
     R1R3NCOCH[NR4C(:X)NR2R5](CH2)nCONHOH [R1, R2 are independently
     (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl,
     heteroaryl, alkylalkenyl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or
     alkylheteroaryl; R3, R4, R5 are independently H or alkyl; X is O or S; n
     is 5 or 6; or stereoisomers, pharmaceutically-acceptable salts, etc.]
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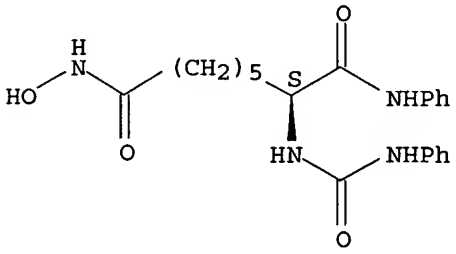
having a urea linkage, that are inhibitors of histone deacetylase (HDAC) and are useful in the prevention and/or treatment of cellular proliferative diseases, e.g., cancer. Thus, (S)-2-(3-phenylureido)octanedioic acid 8-hydroxyamide 1-phenylamide was prepared from (2S)-(tert-butoxycarbonylamino)octanedioic acid 8-Me ester by condensation reactions with aniline and Ph isocyanate, deprotection, and hydroxyamination reactions. In an HDAC1 inhibition in vitro deacetylation assay, several compds. were able to inhibit 50% of the deacetylation reaction at a concentration of .ltorsim. 10 nM.

IT 876054-59-0P 876054-60-3P 876054-61-4P
876054-62-5P 876054-63-6P 876054-64-7P
876054-65-8P 876054-66-9P 876054-67-0P
876054-68-1P 876054-69-2P 876054-70-5P
876054-71-6P 876054-72-7P 876054-73-8P
876054-74-9P 876054-75-0P 876054-76-1P
876054-77-2P 876054-78-3P 876054-79-4P
876054-80-7P 876054-81-8P 876054-82-9P
876054-87-4P 876054-88-5P 876054-89-6P
876054-90-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino hydroxamic acid urea derivs. as histone deacetylase inhibitors)

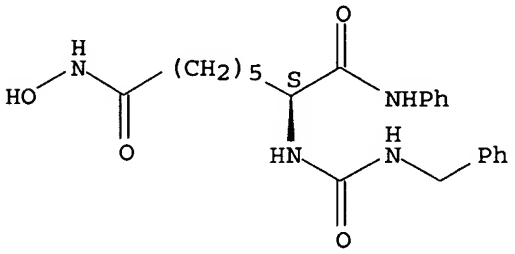
RN 876054-59-0 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[(phenylamino)carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 876054-60-3 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[(phenylmethyl)amino]carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

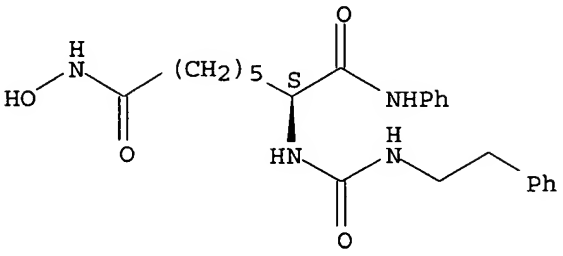
Absolute stereochemistry.



RN 876054-61-4 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[(2-phenylethyl)amino]carbonyl]ami

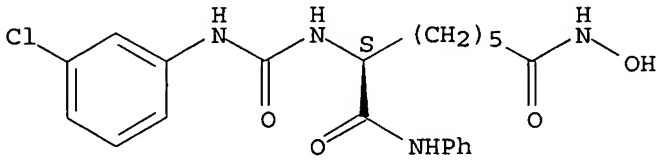
no]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



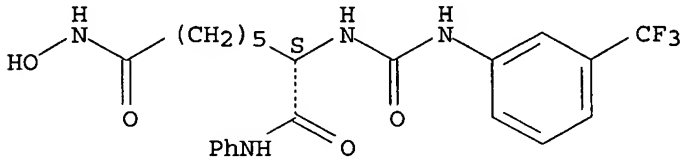
RN 876054-62-5 HCAPLUS
CN Octanediamide, 2-[[[(3-chlorophenyl)amino]carbonyl]amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



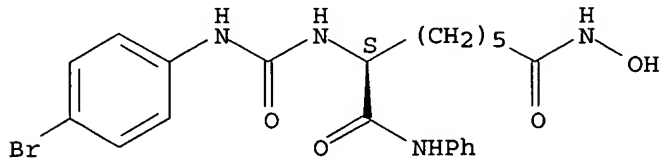
RN 876054-63-6 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



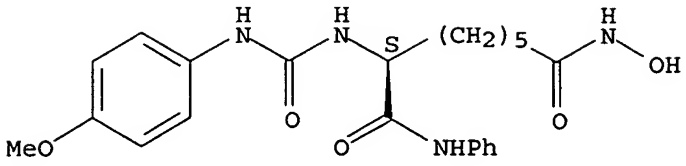
RN 876054-64-7 HCAPLUS
CN Octanediamide, 2-[[[(4-bromophenyl)amino]carbonyl]amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



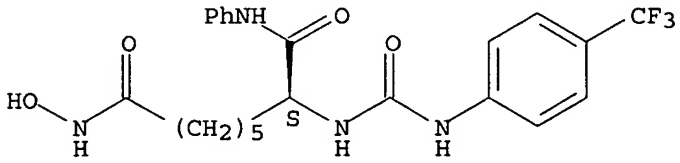
RN 876054-65-8 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[[(4-methoxyphenyl)amino]carbonyl]amino]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



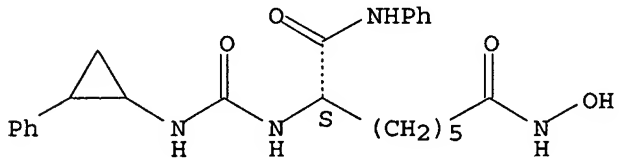
RN 876054-66-9 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[[4-(trifluoromethyl)phenyl]amino]carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



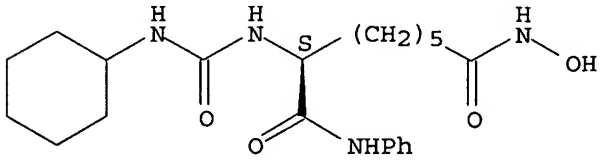
RN 876054-67-0 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[(2-phenylcyclopropyl)amino]carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



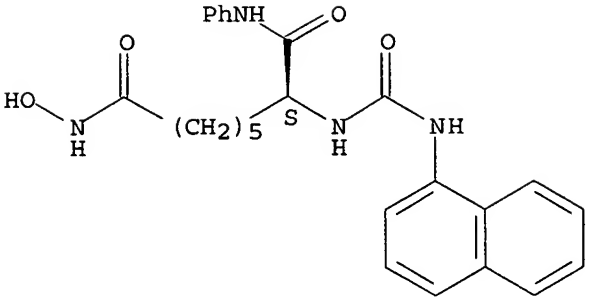
RN 876054-68-1 HCAPLUS
CN Octanediamide, 2-[[(cyclohexylamino)carbonyl]amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 876054-69-2 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[(1-naphthalenylamino)carbonyl]amino]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 876054-70-5 HCAPLUS
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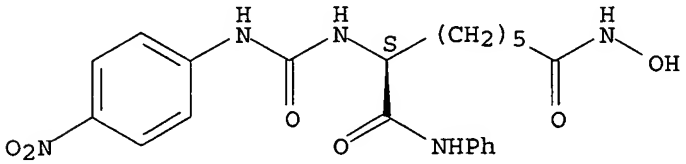
Absolute stereochemistry.



RN 876054-71-6 HCAPLUS
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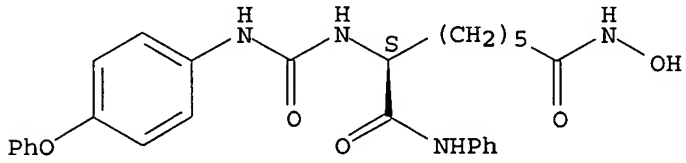
Absolute stereochemistry.



RN 876054-72-7 HCAPLUS
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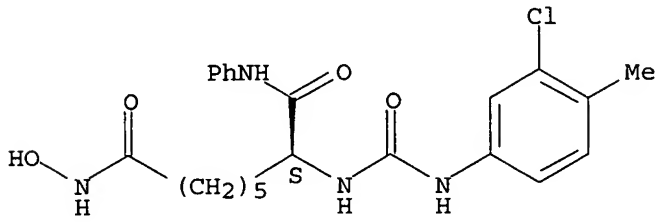
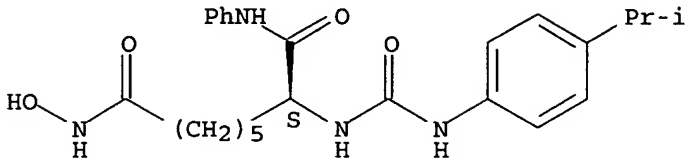
Absolute stereochemistry.



RN 876054-73-8 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[[[4-(1-methylethyl)phenyl]amino]carbonyl]ami

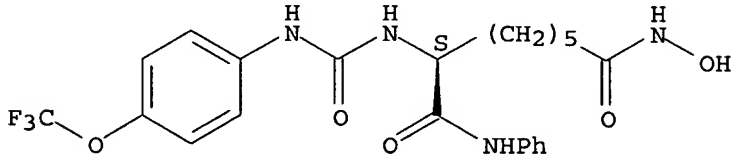
no]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



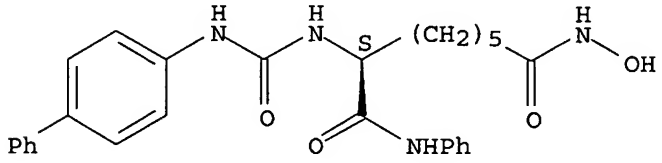
RN 876054-74-9 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 876054-75-0 HCAPLUS
CN Octanediamide, 2-[[([1,1'-biphenyl]-4-ylamino)carbonyl]amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 876054-76-1 HCAPLUS
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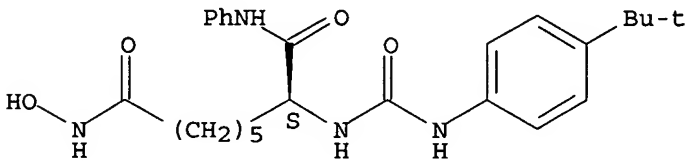
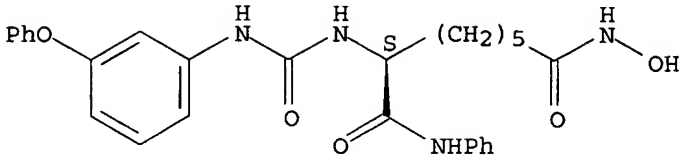
Absolute stereochemistry.



RN 876054-77-2 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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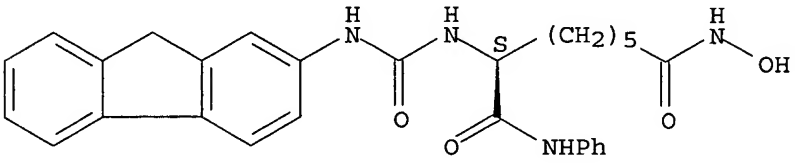
Absolute stereochemistry.



RN 876054-79-4 HCAPLUS
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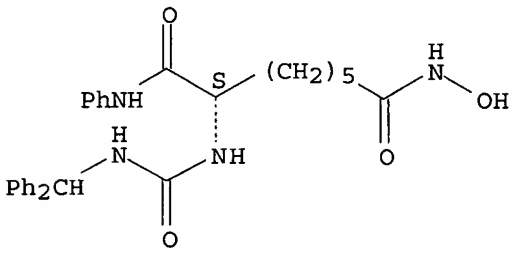
Absolute stereochemistry.



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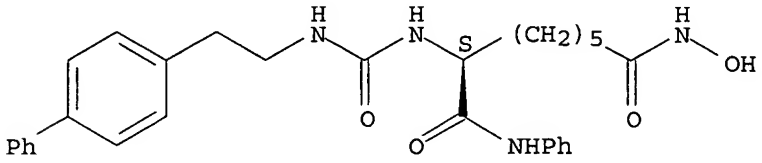
Absolute stereochemistry.



RN 876054-81-8 HCAPLUS
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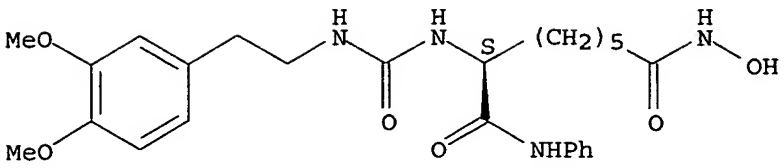
Absolute stereochemistry.



RN 876054-82-9 HCAPLUS
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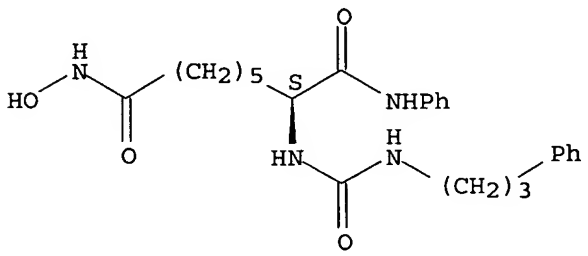
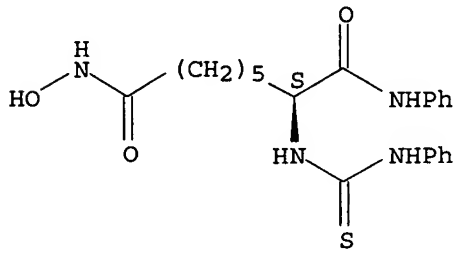
Absolute stereochemistry.



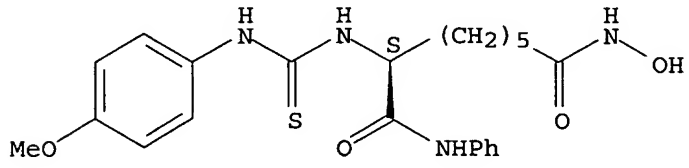
RN 876054-87-4 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[[(phenylamino)thioxomethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



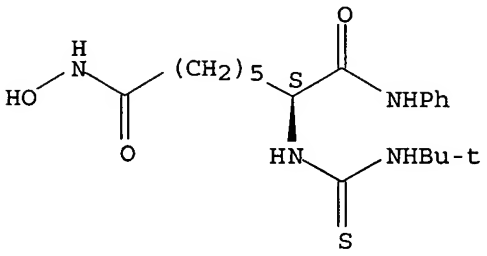
RN 876054-88-5 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[[(4-methoxyphenyl)amino]thioxomethyl]amino]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



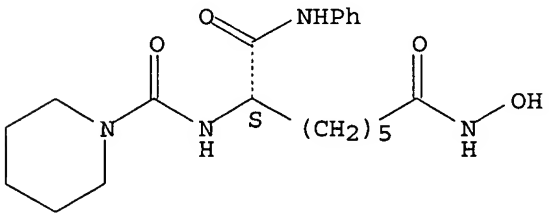
RN 876054-89-6 HCAPLUS
CN Octanediamide, 2-[[[(1,1-dimethylethyl)amino]thioxomethyl]amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

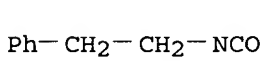


RN 876054-90-9 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(1-piperidinylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 1943-82-4, Phenethyl isocyanate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino hydroxamic acid urea derivs. as histone deacetylase inhibitors)
RN 1943-82-4 HCAPLUS
CN Benzene, (2-isocyanatoethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

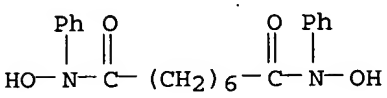
L26 ANSWER 2 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1055402 HCAPLUS
DOCUMENT NUMBER: 144:243764
TITLE: X-ray diffraction studies of some chelate polymers of hydroxamic acid
AUTHOR(S): Ukey, Vaishali V.; Rewatkar, K. G.; Borkar, S. D.; Bonde, A. D.; Naz, S.; Juneja, H. D.
CORPORATE SOURCE: Department of Chemistry, PGTD, Nagpur University, Nagpur, 440033, India
SOURCE: International Journal of Chemical Sciences (2005), 3(2), 229-236
CODEN: IJCSIL; ISSN: 0972-768X
PUBLISHER: Sadguru Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chelate polymers of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) were prepared

with the ligand derived from suberoylbis(N-phenylhydroxamic acid) having equimolar stoichiometry of the cations and ligand. Detailed x-ray diffraction studies were undertaken. These chelate polymers are colored, amorphous solid and highly insol. in aqueous and common organic solvents. From x-ray diffraction data, an orthorhombic crystal system is proposed. The x-ray diffraction data were also used to index the compds. and for determination of various parameters.

IT 89959-39-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactions with transition metal acetates)

RN 89959-39-7 HCAPLUS

CN Octanediamide, N,N'-dihydroxy-N,N'-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:972437 HCAPLUS

DOCUMENT NUMBER: 144:100456

TITLE: Activity of Suberoylanilide Hydroxamic Acid Against Human Breast Cancer Cells with Amplification of Her-2

AUTHOR(S): Bali, Purva; Pranpat, Michael; Swaby, Ramona; Fiskus, Warren; Yamaguchi, Hirohito; Balasis, Maria; Rocha, Kathy; Wang, Hong-Gang; Richon, Victoria; Bhalla, Kapil

CORPORATE SOURCE: Department of Interdisciplinary Oncology, Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, FL, USA

SOURCE: Clinical Cancer Research (2005), 11(17), 6382-6389
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: We determined the effects of suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, on hsp90 and its client proteins Her-2, AKT, and c-Raf, as well as evaluated the cytotoxic effects of cotreatment of SAHA with trastuzumab or docetaxel in human breast cancer BT-474 and SKBR-3 cells containing amplification of Her-2. Exptl. Design: The cells were treated with SAHA (1.0-5.0 μmol/L) and/or trastuzumab (5-40 μg/mL) or docetaxel (5-20 nmol/L). Following this, apoptosis and the levels of p21WAF1, p27KIP1, AKT, c-Raf, and Her-2, as well as of the key regulators of apoptosis were determined Synergistic interaction between drugs was evaluated by median dose-effect anal. Results: Treatment with SAHA up-regulated p21WAF1 and p27KIP1 levels, increased the percentage of cells in G2-M phase of the cell cycle, as well as induced apoptosis in a dose-dependent manner. This was associated with up-regulation of the pro-death Bak and Bim, as well as with attenuation of the levels of Her-2 and XIAP, survivin, Bcl-2, and Bcl-xL proteins. SAHA treatment induced acetylation of hsp90. This reduced the chaperone association of Her-2 with hsp90, promoting polyubiquitylation and degradation of Her-2. SAHA also attenuated the levels of c-Raf and AKT. Cotreatment with SAHA significantly increased trastuzumab

or docetaxel-induced apoptosis of BT-474 and SKBR-3 cells. Addnl., median dose-effect anal. revealed that cotreatment with SAHA and trastuzumab or docetaxel induced synergistic cytotoxic effects against the breast cancer cells. Conclusions: These preclin. findings support the development of SAHA in combination with docetaxel and/or trastuzumab against Her-2-amplified breast cancer.
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

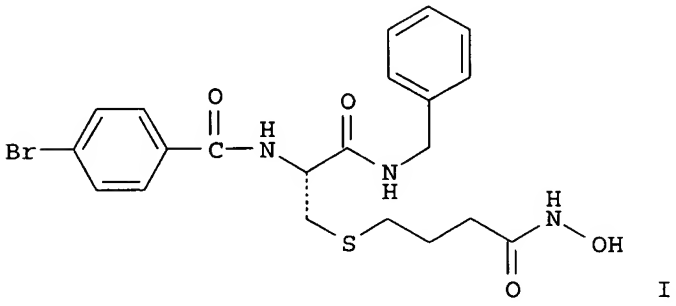
L26 ANSWER 4 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:555185 HCAPLUS
DOCUMENT NUMBER: 143:221971
TITLE: Ras/MAP Kinase pathways are involved in Ras specific apoptosis induced by sodium butyrate
AUTHOR(S): Jung, Ji-Won; Cho, Sung-Dae; Ahn, Nam-Shik; Yang, Se-Ran; Park, Joon-Suk; Jo, Eun-Hye; Hwang, Jae-Woong; Jung, Ji-Youn; Kim, Sung-Hoon; Kang, Kyung-Sun; Lee, Yong-Soon
CORPORATE SOURCE: Department of Veterinary Public Health, College of Veterinary Medicine, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Cancer Letters (Amsterdam, Netherlands) (2005), 225(2), 199-206
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone deacetylase inhibitors such as TSA, SAHA, and NaBu etc. are prospective cancer therapeutics of growing interest. Here, we demonstrated that oncogenic ras-transformed rat liver epithelial (WB-ras) cells were specifically undergone apoptosis by 48 h treatment of NaBu. During this, inhibition of ras proteins, especially farnesylated form of ras, and down-regulation of ERK1/2 were observed, which suggest ras/raf/MEK/ERK down-regulation, while p38 MAP kinase was maintained up-regulated. In addition, up-regulation of pro-apoptotic proteins such as p53 and p21CIP1/WAF1, and down-regulation of cell cycle regulator/anti-apoptotic proteins such as cdk2, -4 and phosphorylated Akt were observed concurrently with an increase in apoptotic cell portion. A phosphatase inhibitor, sodium orthovanadate (SOV), efficiently blocked apoptosis and restored responsible proteins for each phenomenon including ERK1/2 while SB203580, a specific p38 MAP kinase inhibitor, showed minor effect on them. Thus, ras/ERK signaling pathway can be considered in chemotherapeutic strategies of NaBu regardless of its inhibitory action on histone deacetylase.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:490350 HCAPLUS
DOCUMENT NUMBER: 143:26877
TITLE: Preparation of amino acid derivatives as anticancer agents
INVENTOR(S): Fairlie, David; Glenn, Matthew; Kahnberg, Pia
PATENT ASSIGNEE(S): The University of Queensland, Australia
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005051901	A1	20050609	WO 2004-AU1667		20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004293127	A1	20050609	AU 2004-293127		20041126
PRIORITY APPLN. INFO.:			AU 2003-906633	A	20031128
			WO 2004-AU1667	W	20041126

OTHER SOURCE(S): MARPAT 143:26877

GI



I

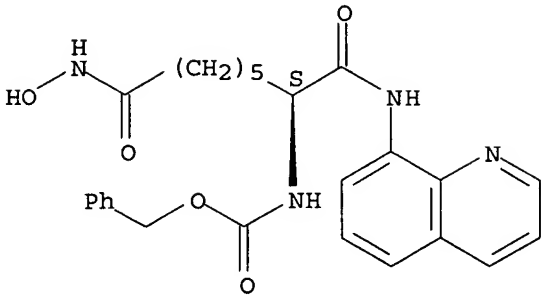
AB The invention provides compds. R7-X-NR6CH(CH2-Z-R1-M)CO-Y [Z is S or CH2; R1 is a linking moiety; M is a zinc-binding moiety containing at least one heteroatom; R6 is H, (un)substituted alkyl, alkenyl, alkynyl or a protecting group; X is CH2, CO, CS or SO2; Y is NR4R5, OR4, SR4, CH2R4, CHR4R5, CR42R5, PHR4 or PR4R5, where R4 and R4 are independently alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl or heterocycloalkyl which may be substituted, e.g., by carbamoyl groups], including their pharmaceutically-acceptable derivs., salts, racemates, isomers or tautomers, for use in the treatment of cancer. Thus, L-cysteine derivative I, prepared via amidation reactions, showed IC50 = 0.02 ± 0.1 μM (selectivity 4.2) against human cancer cell (MM96L, melanoma).

IT 329967-01-3P 329967-03-5P 853153-50-1P
853153-56-7P 853153-70-5P 853153-71-6P
853153-72-7P 853153-73-8P 853153-74-9P
853153-75-0P 853153-81-8P 853153-82-9P
853154-30-0P 853154-31-1P 853154-32-2P
853154-33-3P 853154-34-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as anticancer agents)

RN 329967-01-3 HCAPLUS

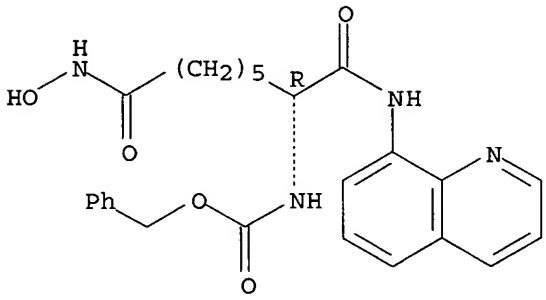
CN Carbamic acid, [(1S)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



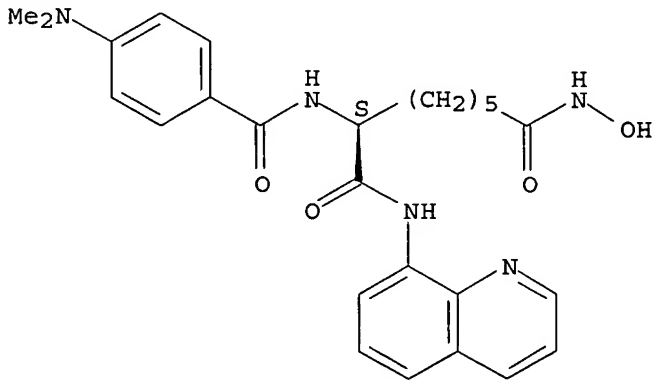
RN 329967-03-5 HCAPLUS
CN Carbamic acid, [(1R)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 853153-50-1 HCAPLUS
CN Octanediamide, 2-[[4-(dimethylamino)benzoyl]amino]-N8-hydroxy-N1-8-quinolinyl-, (2S)- (9CI) (CA INDEX NAME)

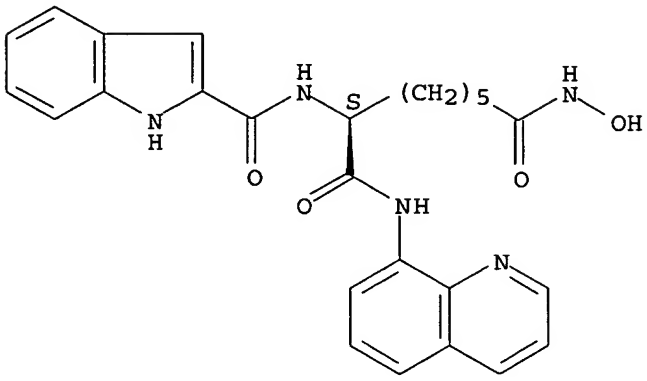
Absolute stereochemistry.



RN 853153-56-7 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[(1H-indol-2-ylcarbonyl)amino]-N1-8-quinolinyl-

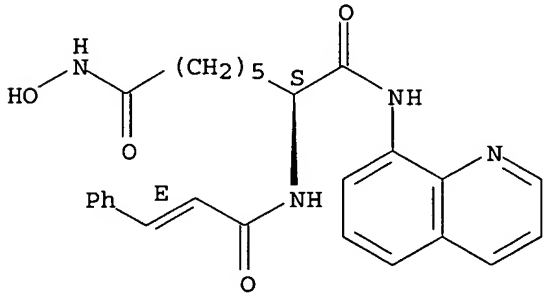
, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



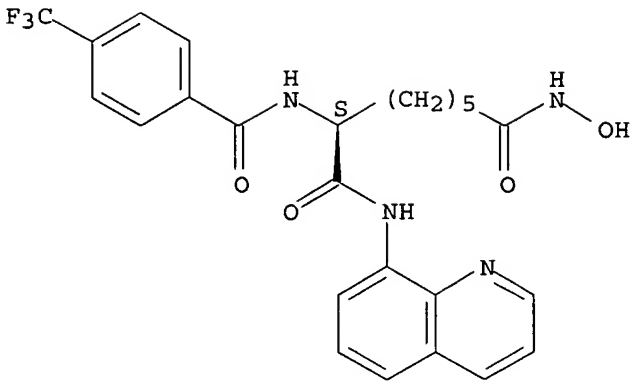
RN 853153-70-5 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[(2E)-1-oxo-3-phenyl-2-propenyl]amino]-N1-8-quinolinyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



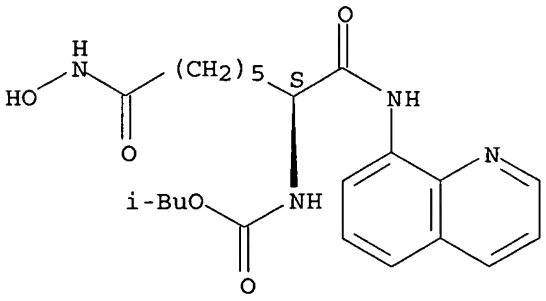
RN 853153-71-6 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-8-quinolinyl-2-[[4-(trifluoromethyl)benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



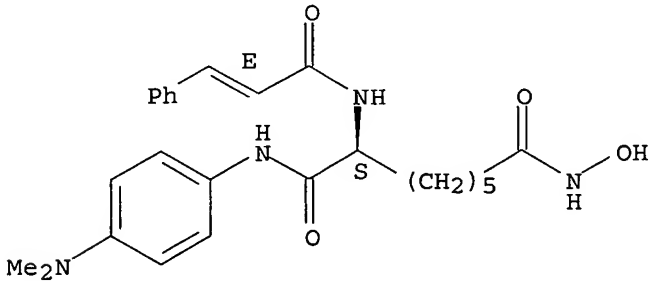
RN 853153-72-7 HCAPLUS
CN Carbamic acid, [(1S)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



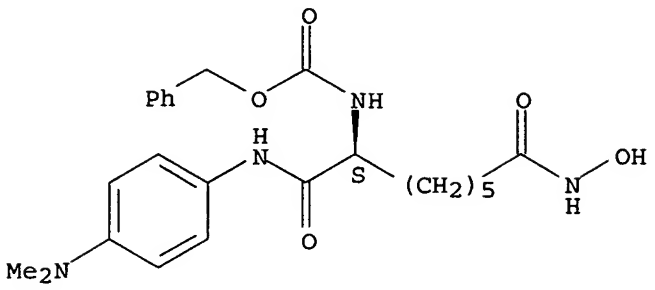
RN 853153-73-8 HCAPLUS
CN Octanediamide, N1-[4-(dimethylamino)phenyl]-N8-hydroxy-2-[[(2E)-1-oxo-3-phenyl-2-propenyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



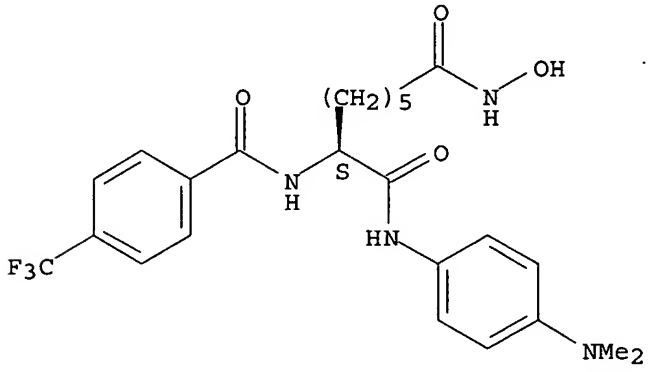
RN 853153-74-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[4-(dimethylamino)phenyl]amino]carbonyl]-7-(hydroxyamino)-7-oxoheptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



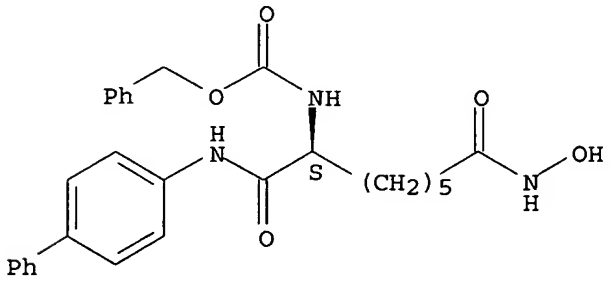
RN 853153-75-0 HCAPLUS
CN Octanediamide, N1-[4-(dimethylamino)phenyl]-N8-hydroxy-2-[[4-(trifluoromethyl)benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



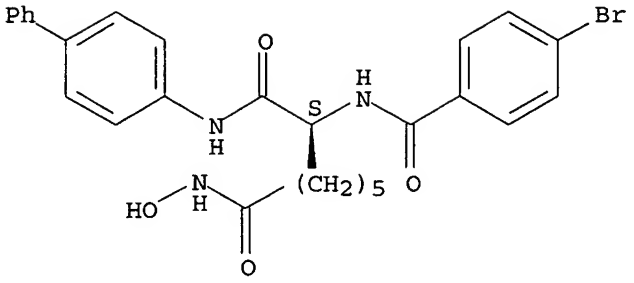
RN 853153-81-8 HCAPLUS
CN Carbamic acid, [(1S)-1-[([1,1'-biphenyl]-4-ylamino)carbonyl]-7-(hydroxyamino)-7-oxoheptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



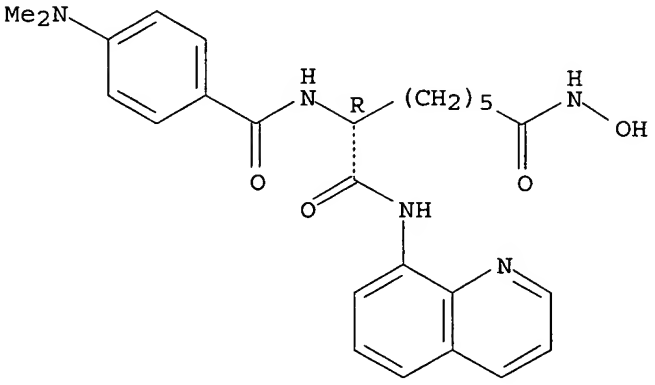
RN 853153-82-9 HCAPLUS
CN Octanediamide, N1-[1,1'-biphenyl]-4-yl-2-[(4-bromobenzoyl)amino]-N8-hydroxy-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



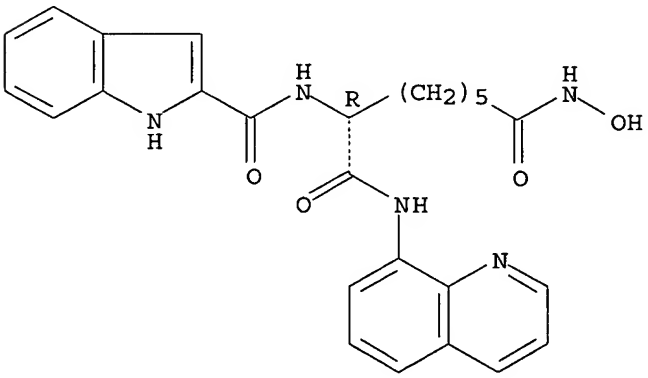
RN 853154-30-0 HCAPLUS
CN Octanediamide, 2-[[4-(dimethylamino)benzoyl]amino]-N8-hydroxy-N1-8-quinolinyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



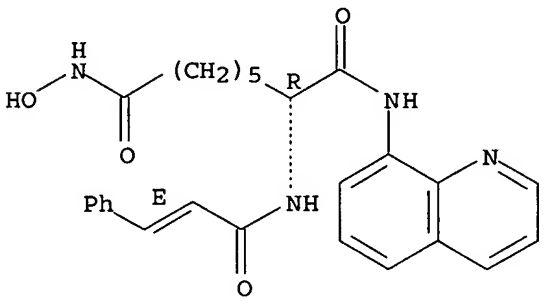
RN 853154-31-1 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[(1H-indol-2-ylcarbonyl)amino]-N1-8-quinolinyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



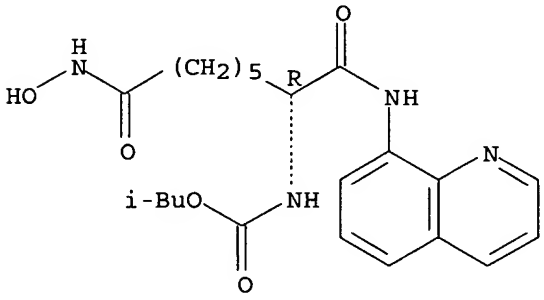
RN 853154-32-2 HCAPLUS
CN Octanediamide, N8-hydroxy-2-[[(2E)-1-oxo-3-phenyl-2-propenyl]amino]-N1-8-quinolinyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



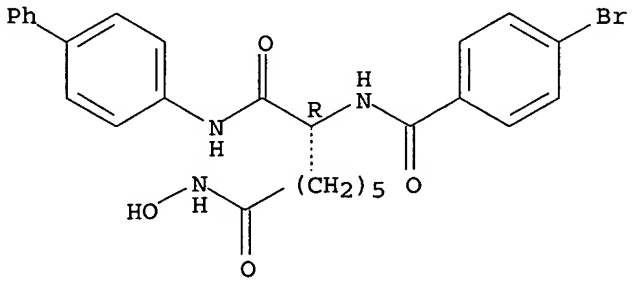
RN 853154-33-3 HCAPLUS
CN Carbamic acid, [(1R)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 853154-34-4 HCAPLUS
CN Octanediamide, N1-[1,1'-biphenyl]-4-yl-2-[(4-bromobenzoyl)amino]-N8-hydroxy-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 4048-33-3, 6-Amino 1 hexanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as anticancer agents)
RN 4048-33-3 HCAPLUS
CN 1-Hexanol, 6-amino- (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-(CH_2)_6-OH$

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:356029 HCAPLUS
DOCUMENT NUMBER: 143:225053
TITLE: Modulation of radiation response by histone deacetylase inhibition
AUTHOR(S): Chinnaiyan, Prakash; Vallabhaneni, Geetha; Armstrong, Eric; Huang, Shyh-Min; Harari, Paul M.
CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin School of Medicine and Comprehensive Cancer Center, Madison, WI, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2005), 62(1), 223-229
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Histone deacetylase (HDAC) inhibitors, which modulate chromatin structure and gene expression, represent a class of anticancer agents that hold particular potential as radiation sensitizers. In this study, we examine the capacity of the HDAC inhibitor suberoylanilide hydroxamic acid (SAHA) to modulate radiation response in human tumor cell lines and explore potential mechanisms underlying these interactions. Cell proliferation: Exponentially growing tumor cells were incubated in medium containing 0-10 μM of SAHA for 72 h. Cells were fixed/stained with crystal violet to estimate cell viability. Apoptosis: Caspase activity was analyzed by fluorescence spectroscopy using a fluorescein labeled pan-caspase inhibitor. Cells were harvested after 48 h of exposure to SAHA (1.0 μM), radiation (6 Gy), or the combination. Whole cell lysates were evaluated for poly(ADP-ribose) polymerase (PARP) cleavage by western blot anal. Radiation survival: Cells were exposed to varying doses of radiation ± 3 days pretreatment with SAHA (0.75-1.0 μM). After incubation intervals of 14-21 days, colonies were stained with crystal violet and manually counted. Immunocytochem.: Cells were grown and treated in chamber slides. At specified times after treatment with SAHA, cells were fixed in paraformaldehyde, permeabilized in methanol, and probed with primary and secondary antibody solns. Slides were analyzed using an epifluorescent microscope. SAHA induced a dose-dependent inhibition of proliferation in human prostate (DU145) and glioma (U373vIII) cancer cell lines. Exposure to SAHA enhanced radiation-induced apoptosis as measured by caspase activity ($p < 0.05$) and PARP cleavage. The impact of SAHA on radiation response was further characterized using clonogenic survival anal., which demonstrated that treatment with SAHA reduced tumor survival after radiation exposure. We identified several oncoproteins and DNA damage repair proteins (epidermal growth factor receptor, AKT, DNA-PK, and Rad51) that show differential expression after exposure to SAHA. These proteins may contribute to mechanistic synergy between HDAC inhibition and radiation response. These preclin. results suggest that treatment with the HDAC inhibitor SAHA can enhance radiation-induced cytotoxicity in human prostate and glioma cells. We are examining the capacity of HDAC inhibitors to modulate radiation response and

tumor control in animal xenograft model systems to strengthen the rationale for future clin. trial exploration.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:232565 HCAPLUS
DOCUMENT NUMBER: 142:309871
TITLE: Combination methods of treating cancer
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Marks, Paul A.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.; Rifkind, Richard A.
PATENT ASSIGNEE(S): Aton Pharma, Inc., USA; Sloan-Kettering Institute for Cancer Research
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023179	A2	20050317	WO 2004-US26161	20040812
WO 2005023179	A3	20050616		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004270150	A2	20050317	AU 2004-270150	20040812
AU 2004270150	A1	20050317		
CA 2535889	AA	20050317	CA 2004-2535889	20040812
EP 1667680	A2	20060614	EP 2004-780925	20040812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

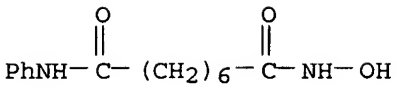
PRIORITY APPLN. INFO.: US 2003-498803P P 20030829
WO 2004-US26161 W 20040812

OTHER SOURCE(S): MARPAT 142:309871

AB The present invention relates to a method of treating cancer in a subject in need thereof, by administering to a subject in need thereof a first amount of a histone deacetylase (HDAC) inhibitor or a pharmaceutically acceptable salt or hydrate thereof, in a first treatment procedure, and a second amount of an anti-cancer agent in a second treatment procedure. The first and second amts. together comprise a therapeutically effective amount The effect of the HDAC inhibitor and the anti-cancer agent may be additive or synergistic.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for cancer)

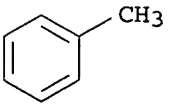
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



L26 ANSWER 8 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:223713 HCAPLUS
DOCUMENT NUMBER: 143:268677
TITLE: Catalytic reactions of post-consumer polymer waste over fluidised cracking catalysts for producing hydrocarbons
AUTHOR(S): Lin, Y.-H.; Yang, M.-H.
CORPORATE SOURCE: Department of Biochemical Engineering and Graduate Institute of Environmental Polymeric Materials, Kao Yuan Institute of Technology, Kaohsiung, 821, Taiwan
SOURCE: Journal of Molecular Catalysis A: Chemical (2005), 231(1-2), 113-122
CODEN: JMCCF2; ISSN: 1381-1169
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A post-consumer polymer mixture of polyethylene, polypropylene, polystyrene, and poly(vinyl chloride) (PE/PP/PS/PVC) was pyrolyzed over catalysts using a laboratory fluidised-bed reactor operating isothermally at ambient pressure. The effects of reaction conditions including catalyst, temperature, ratio of commingled polymer to catalyst feed and flow rate of fluidizing gas were examined The yield of volatile hydrocarbons for zeolitic catalysts (HZSM-5 > HUSY ≈ HMOR) was higher than that from SAHA ≈ MCM-41 catalysts. Product distributions with HZSM-5 contained more olefinic materials with about 60% C3-C5 hydrocarbons. However, both HMOR and HUSY produced more paraffinic streams with large amts. of butane (C4). The larger pore zeolites (HUSY and HMOR) showed deactivation in contrast to the more restrictive HZSM-5. MCM-41 and SAHA showed the lowest conversion and generated an olefin-rich product of C3-C7 compds. The selectivity could be further influenced by changes in reactor conditions. Valuable hydrocarbons of olefins and iso-olefins were produced by low temps. and short contact time.

IT 108-88-3P, Toluene, preparation
RL: IMF (Industrial manufacture); PREP (Preparation)
(activity of zeolite cracking catalysts in pyrolysis of post-consumer polymer wastes in fluidized bed reactor to obtain hydrocarbons)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:122804 HCAPLUS
DOCUMENT NUMBER: 142:219054

TITLE: Preparation of hydroxyamides and mercaptoacetamides as histone deacetylase inhibitors for treatment of neurological diseases and cancer

INVENTOR(S): Kozikowski, Alan P.; Chen, Bin
PATENT ASSIGNEE(S): USA

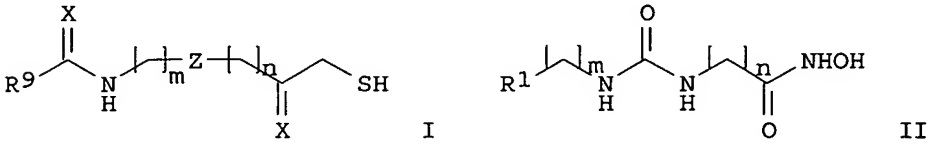
SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 614,498.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005032831	A1	20050210	US 2004-843229	20040511
US 2005014839	A1	20050120	US 2003-614498	20030707
CA 2531661	AA	20050127	CA 2004-2531661	20040707
WO 2005007091	A2	20050127	WO 2004-US21663	20040707
WO 2005007091	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1644323	A2	20060412	EP 2004-777648	20040707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:
US 2003-614498 A2 20030707
US 2004-843229 A 20040511
WO 2004-US21663 W 20040707

OTHER SOURCE(S): MARPAT 142:219054

GI



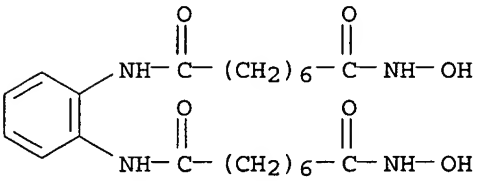
I II

AB The title mercaptoacetamides I [X = O, S; Z = a bond, (un)substituted Ph, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl; R9 = (un)substituted Ph, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl; m, n = 0-5] and hydroxyamides II [R1 = (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl; m, n = 1-10], useful as HDAC inhibitors, were prepared E.g., a 3-step synthesis of 4-[3-(4-dimethylaminobenzyl)ureido]-N-hydroxybutyramide, starting from benzyl 4-aminobutyrate toluene-4-sulfonic acid, was given. The invention provides methods for treating cancer and neurol. diseases. Methods of sensitizing a cancer cell to the cytotoxic effects of radiotherapy are also provided. Thus, numerous compds. I and II were tested in vitro for inhibition of HDAC and for sensitizing

radiation resistant squamous carcinoma cell line SQ-20B to gamma radiation. One of the more effective inhibitors was 7-[3-(4-dimethylaminobenzyl)ureido]heptanoic acid hydroxyamide. The pharmaceutical composition comprising the compound I is also disclosed.

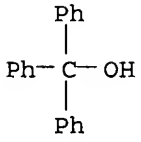
IT 827036-70-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxyamides and mercaptoacetamides as histone deacetylase inhibitors for treatment of neurol. diseases and cancer)

RN 827036-70-4 HCAPLUS
CN Octanediamide, N,N''-1,2-phenylenebis[N'-hydroxy- (9CI) (CA INDEX NAME)

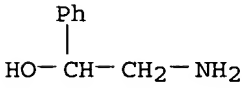


IT 76-84-6, Triphenylmethanol 7568-93-6, 2-Amino-1-phenylethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydroxyamides and mercaptoacetamides as histone deacetylase inhibitors for treatment of neurol. diseases and cancer)

RN 76-84-6 HCAPLUS
CN Benzenemethanol, α,α-diphenyl- (9CI) (CA INDEX NAME)



RN 7568-93-6 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)- (9CI) (CA INDEX NAME)



L26 ANSWER 10 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:71067 HCAPLUS
DOCUMENT NUMBER: 142:150831
TITLE: Histone deacetylase inhibitors for treatment of neurological diseases and cancer
INVENTOR(S): Kozikowski, Alan P.; Dritschilo, Anatoly; Jung, Mira; Petukhov, Pavel; Chen, Bin
PATENT ASSIGNEE(S): Georgetown University, USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007091	A2	20050127	WO 2004-US21663	20040707
WO 2005007091	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005014839	A1	20050120	US 2003-614498	20030707
US 2005032831	A1	20050210	US 2004-843229	20040511
CA 2531661	AA	20050127	CA 2004-2531661	20040707
EP 1644323	A2	20060412	EP 2004-777648	20040707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

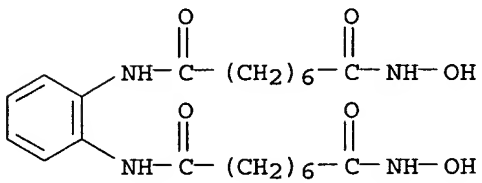
PRIORITY APPLN. INFO.:
US 2003-614498 A 20030707
US 2004-843229 A 20040511
WO 2004-US21663 W 20040707

OTHER SOURCE(S): CASREACT 142:150831; MARPAT 142:150831

AB One aspect of the invention relates to HDAC inhibitors. Methods of sensitizing a cancer cell to the cytotoxic effects of radiotherapy are also provided. The invention also provides methods for treating cancer and methods for treating neurol. diseases. Thus, numerous HDAC inhibitors were synthesized and tested in vitro for inhibition of HDAC and for sensitizing radiation resistant squamous carcinoma cell line SQ-20B to gamma radiation. One of the more effective inhibitors was 7-[3-(4-dimethylaminobenzyl)ureido]heptanoic acid hydroxyamide.

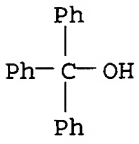
IT 827036-70-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(histone deacetylase inhibitors for treatment of neurol. diseases and cancer)

RN 827036-70-4 HCAPLUS
CN Octanediamide, N,N''-1,2-phenylenebis[N'-hydroxy- (9CI) (CA INDEX NAME)

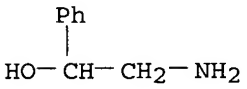


IT 76-84-6, Triphenylmethanol 7568-93-6, 2-Amino-1-phenylethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(histone deacetylase inhibitors for treatment of neurol. diseases and

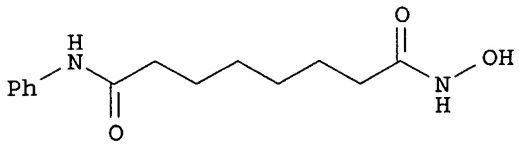
cancer)
RN 76-84-6 HCAPLUS
CN Benzenemethanol, α,α-diphenyl- (9CI) (CA INDEX NAME)



RN 7568-93-6 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)- (9CI) (CA INDEX NAME)



L26 ANSWER 11 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:64339 HCAPLUS
DOCUMENT NUMBER: 142:316538
TITLE: Novel Inhibitors of Human Histone Deacetylases: Design, Synthesis, Enzyme Inhibition, and Cancer Cell Growth Inhibition of SAHA-Based Non-hydroxamates
AUTHOR(S): Suzuki, Takayoshi; Nagano, Yuki; Kouketsu, Akiyasu; Matsuura, Azusa; Maruyama, Sakiko; Kurotaki, Mineko; Nakagawa, Hidehiko; Miyata, Naoki
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Nagoya City University, Mizuho, Nagoya, Aichi, 467-8603, Japan
SOURCE: Journal of Medicinal Chemistry (2005), 48(4), 1019-1032
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:316538
GI



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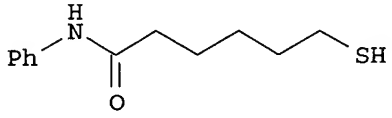


II

AB To find novel non-hydroxamate histone deacetylase (HDAC) inhibitors, a series of compds. modeled after suberoylanilide hydroxamic acid (SAHA) was designed and synthesized. The compds. prepared for this study were analogs and derivs. of N-hydroxy-N'-(phenyl)octanediamide (SAHA) (I). In this series, 7-mercapto-N-(phenyl)heptanamide (II), in which the hydroxamic acid of SAHA is replaced by a thiol, was found to be as potent as SAHA, and optimization of this series led to the identification of HDAC inhibitors more potent than SAHA. In cancer cell growth inhibition assay, an S-isobutyryl derivative showed strong activity, and its potency was comparable to that of SAHA. The cancer cell growth inhibitory activity was verified to be the result of histone hyperacetylation and subsequent induction of p21WAF1/CIP1 by Western blot anal. Kinetic enzyme assay and mol. modeling suggest the thiol formed by enzymic hydrolysis within the cell interacts with the zinc ion in the active site of HDACs.

IT 4048-33-3, 6-Amino-1-hexanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 7-(mercapto)--N-(phenyl)heptanamide (suberoylanilide hydroxamic acid) analog and study of its binding to histone deacetylase docking site)

RN 4048-33-3 HCAPLUS

CN 1-Hexanol, 6-amino- (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-(CH_2)_6-OH$

IT 4286-55-9, 6-Bromo-1-hexanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-hydroxy-N'-(phenyl)octanediamide (suberoylanilide hydroxamic acid) analogs using (bromo)hexanol as starting material)

RN 4286-55-9 HCAPLUS

CN 1-Hexanol, 6-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

$Br-(CH_2)_6-OH$

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:59981 HCAPLUS

DOCUMENT NUMBER: 142:134325

TITLE: Preparation of ω-ureido alkanohydroxamic acid and related urea derivatives as histone deacetylase inhibitors

INVENTOR(S): Kozikowski, Alan P.; Dritschilo, Anatoly; Jung, Mira; Petukhov, Pavel A.; Chen, Bin

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

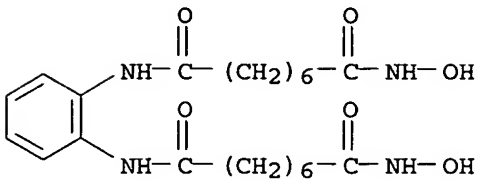
US 2005014839 A1 20050120 US 2003-614498 20030707
US 2005032831 A1 20050210 US 2004-843229 20040511
CA 2531661 AA 20050127 CA 2004-2531661 20040707
WO 2005007091 A2 20050127 WO 2004-US21663 20040707
WO 2005007091 A3 20050428
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1644323 A2 20060412 EP 2004-777648 20040707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRIORITY APPLN. INFO.: US 2003-614498 A2 20030707
US 2004-843229 A 20040511
WO 2004-US21663 W 20040707

OTHER SOURCE(S): MARPAT 142:134325

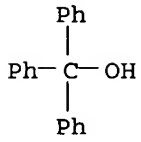
AB Urea derivs. of formula R1(CH2)mNHCONH(CH2)nY [Y = CONHOH, COCH2SH, NHCOCH2SH; R1 = C1-6 alkyl, aryl, C3-7 cycloalkyl, or -3- to 10-membered heterocycle, any of which may be unsubstituted or substituted with one or more of the following groups including halo, C1-6 alkyl, C1-6 alkoxy, OH, cyano, CO2R', -OC(O)R', NHR', N(R')2, -NHC(O)R', or -C(O)NHR' groups; wherein R' is H or unsubstituted C1-6, with the proviso that when n is 2, R1 cannot be C3-7 cycloalkyl or 3- to 10-membered heterocycle; m, n = an integer ranging from 1-10] or pharmaceutically acceptable salts thereof are prepared The invention provides novel classes of histone deacetylase (HDAC) inhibitors. Methods of sensitizing a cancer cell to the cytotoxic effects of radiotherapy are also provided as well as methods for treating cancer and methods for treating neurol. diseases. Addnl., the invention further provides pharmaceutical compns. comprising an HDAC inhibitor of the invention, and kits comprising a container containing an HDAC inhibitor of the invention. The above cancer is Non-Hodgkin's lymphoma, Hodgkin's disease, Ewing's sarcoma, testicular cancer, prostate cancer, larynx cancer, cervical cancer, nasopharynx cancer, breast cancer, col on cancer, pancreatic cancer, head and neck cancer, esophageal cancer, rectal cancer, small-cell lung cancer, non-small cell lung cancer, brain cancer, or a CNS neoplasm. Said disease of the central nervous system is Huntington's disease, lupus, or schizophrenia. Thus, hydrogenolysis of 4-[N'-(4-dimethylaminobenzyl)ureido]butyric acid benzyl ester over 10% Pd-C in MeOH under a hydrogen atmospheric for 18 h followed by condensation benzyloxyamine hydrochloride using EDCI in the presence of Et3N at room temperature for 18 h gave N-Benzyloxy-4-[N'-(4-dimethylaminobenzyl)ureido]butyramide which underwent similar hydrogenolysis to give 4-[N'-(4-Dimethylaminobenzyl)ureido]-N-hydroxybutyramide (I). I and 8-[N'-(4-dimethylaminobenzyl)ureido]octanoic acid hydroxyamide inhibited histone deacetylase with IC50 of 800 and 700 nM, resp.

IT 827036-70-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. as histone deacetylase inhibitors and for sensitizing cancer cell to cytotoxic effects of radiotherapy and treating cancer and neurol. diseases)

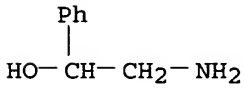
RN 827036-70-4 HCAPLUS
CN Octanediamide, N,N''-1,2-phenylenebis[N'-hydroxy- (9CI) (CA INDEX NAME)



IT 76-84-6, Triphenylmethanol 7568-93-6,
2-Amino-1-phenylethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of urea derivs. as histone deacetylase inhibitors and for sensitizing cancer cell to cytotoxic effects of radiotherapy and treating cancer and neurol. diseases)
RN 76-84-6 HCAPLUS
CN Benzenemethanol, α,α-diphenyl- (9CI) (CA INDEX NAME)



RN 7568-93-6 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)- (9CI) (CA INDEX NAME)



L26 ANSWER 13 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:40767 HCAPLUS
TITLE: New Drugs in Cancer Therapy, National Tumor Institute, Naples, 17-18 June 2004
AUTHOR(S): Caponigro, Francesco; Basile, Maria; de Rosa, Vincenzo; Normanno, Nicola
CORPORATE SOURCE: National Tumor Institute, Fondazione 'G. Pascale', Naples, Italy
SOURCE: Anti-Cancer Drugs (2005), 16(2), 211-221
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; News Announcement
LANGUAGE: English
AB An international meeting on 'New Drugs in Cancer Therapy' was held at the National Tumor Institute of Naples, on 17-18 June 2004. The first session of the meeting focused on analogs of conventional anti-cancer drugs, such as taxanes, platinum compds., anthracyclines and topoisomerase I inhibitors. The data of a phase II trial of BMS-247550, an epothilone B analog, in patients with renal cell carcinoma were reported. Data were also presented on BBR-3464, a trinucleate platinum analog which was

developed on the grounds of greater potency, a more rapid rate of DNA binding and the ability to induce apoptosis regardless of the p53 status of the cell. Pegylated-coated liposomal formulation doxorubicin (Caelyx) has shown efficacy in metastatic breast cancer and in advanced ovarian cancer; sabarubicin is a third-generation anthracycline with equal or superior potency to doxorubicin or idarubicin in a variety of human tumor cell lines of different histotypes. The main mechanisms of resistance to topoisomerase I inhibitors were discussed; data on diflomotecan were reported, showing a narrow therapeutic index of the drug. The second session of the meeting focused on the ErbB family as a target for anti-cancer therapy. Recent evidence of a correlation between epidermal growth factor receptor (EGFR) mutations at exons 18-21 and clin. response of advanced non-small cell lung cancer to gefitinib therapy was commented on. The issue of the association between ErbB2 expression and gefitinib activity was addressed, while clin. data of a phase II study of gefitinib in advanced breast cancer were presented. Monoclonal antibodies targeting EGFR represent another worthwhile way to interfere with EGFR-driven signal transduction. Cetuximab is reaching market registration in advanced colorectal cancer; in particular, due to the results of the BOND study. The recently presented results of the Bonner study strongly support the activity of this drug in head and neck cancer. A step forward in the research on anti-EGFR monoclonal antibodies may be represented by humanized monoclonal antibodies, such as EMD 72000 and ABX-EGF. Imatinib mesylate is probably the most outstanding example of an effective targeted therapy-its activity in gastrointestinal stromal tumors was so exciting that the drug reached the market without undergoing phase III evaluation. The third session of the meeting was on angiogenesis inhibitors. Drugs may interfere with the angiogenic process via different mechanisms and there is a sound rationale for combining anti-angiogenic agents with chemotherapy or multiple anti-angiogenic strategies. Clin. results obtained with direct anti-angiogenic agents have been neg. up to now, but some exciting results have been seen with bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF). A few VEGF-tyrosine kinase inhibiting small mols., such as ZD6474, AZD2171 and PTK/ZK, are undergoing clin. trials. The fourth session of the meeting was on interference with intracellular signal transduction. Farnesyl transferase inhibitors exert their action by interfering with either pro-Ras or RhoB farnesylation. Several clin. studies of different phases with compds. belonging to this class have been carried out, either alone or in combination with chemotherapy; unfortunately, all of them have turned out to be neg. Cell cycle inhibitors, such as CYC-202 and BMS-387032, represent a class of interesting compds. which are in the early phase of development and whose clin. results are eagerly awaited. Another strategy to achieve cell cycle inhibition is to target heat shock protein 90, a mol. chaperone required for protein folding. Clin. data on depsipeptide, a histone deacetylase (HDAC) inhibitor with activity in T cell lymphoma, were presented. Suberoylanilide hydroxamic acid is another small mol. weight inhibitor of HDAC activity. Phase I/II clin. trials have shown low toxicity and evidence of anti-tumor activity; on the other hand, this compound has potential for synergism with radiotherapy, chemotherapy and biologicals.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 14 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:669118 HCAPLUS
DOCUMENT NUMBER: 142:86023
TITLE: Modulation of pro- and anti-apoptotic factors in human melanoma cells exposed to histone deacetylase inhibitors

AUTHOR(S): Facchetti, F.; Previdi, S.; Ballarini, M.; Minucci, S.; Perego, P.; La Porta, C. A. M.
CORPORATE SOURCE: Department of Biomolecular Sciences and Biotechnology, University of Milan, Italy
SOURCE: Apoptosis (2004), 9(5), 573-582
CODEN: APOPFN; ISSN: 1360-8185
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Valproic acid (VPA, 2-propylpentanoic acid) is an established drug in the long-term therapy of epilepsy. Recently, VPA was demonstrated to inhibit histone deacetylases (HDACs) class I enzyme at therapeutically relevant concns., thereby, mimicking the prototypical histone deacetylase inhibitors, trichostatin A (TSA) or suberoylanilide hydroxamic acid (SAHA). In the present study, we investigated the cellular effects of VPA, TSA and SAHA on four human melanoma cell lines (WM115, WM266, A375, SK-Mel28) with particular reference to the modulation of regulators of apoptosis, including Bcl-2, BclXL, Mcl-1, Apaf-1, BclXs, NOXA, TRAIL-R1, TRAIL-R2, caspase 8, and survivin. Firstly, we found that VPA induced apoptosis in two of the four human melanoma cell lines, while both TSA and SAHA exhibited an antiproliferative and apoptotic effects in all four cell lines, a different expression of Bcl-2 and BclXL/S occurred. On the other hand, SAHA and VPA modulated differently pro- and anti-apoptotic factors. In particular, the treatment with VPA enhanced the level of expression of survivin only in VPA-resistant cell lines, whereas down-regulation of survivin was induced by VPA and SAHA in VPA-sensitive cells. In the latter, since activation of caspase 8 was documented, a receptor-mediated apoptosis was suggested. Taken together, our results suggest that HDAC inhibitors may represent a promising therapeutic strategy to treat melanoma.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 15 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:513346 HCAPLUS
DOCUMENT NUMBER: 141:59733
TITLE: Polymorphs of suberoylanilide hydroxamic acid, method of producing the same, and pharmaceutical composition containing the same
INVENTOR(S): Miller, Thomas A.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Ser. No. 379,149.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

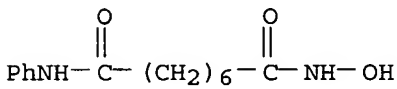
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004122101	A1	20040624	US 2003-600132		20030619
US 2004072735	A1	20040415	US 2003-379149		20030304
PRIORITY APPLN. INFO.:			US 2002-361759P	P	20020304
			US 2003-379149	A2	20030304

AB The present invention provides methods of selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of

pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the present invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The present invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. The present invention also provides a novel Form I polymorph of SAHA , characterized by a unique X-ray diffraction pattern and Differential Scanning Calorimetry profile, as well a unique crystalline structure.

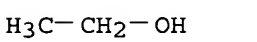
IT 149647-78-9P, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PKT (Pharmacokinetics); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(polymorphs of suberoylanilide hydroxamic acid, method of producing the same, and pharmaceutical composition containing the same)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)

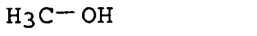


IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses
RL: NUU (Other use, unclassified); USES (Uses)
(recrystn. with; polymorphs of suberoylanilide hydroxamic acid, method of producing the same, and pharmaceutical composition containing the same)

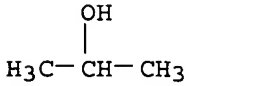
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



RN 67-63-0 HCAPLUS
CN 2-Propanol (9CI) (CA INDEX NAME)

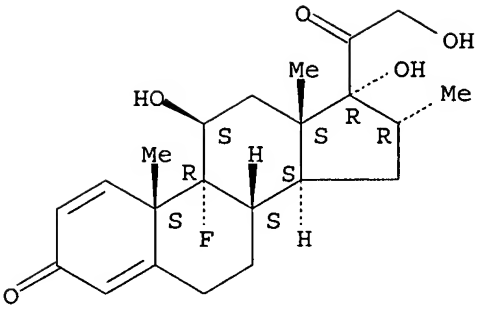


L26 ANSWER 16 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:446456 HCAPLUS
DOCUMENT NUMBER: 142:32521
TITLE: Synergistic induction of oxidative injury and apoptosis in human multiple myeloma cells by the proteasome inhibitor bortezomib and histone deacetylase inhibitors
AUTHOR(S): Pei, Xin-Yan; Dai, Yun; Grant, Steven
CORPORATE SOURCE: Department of Medicine, Virginia Commonwealth University, Richmond, VA, USA
SOURCE: Clinical Cancer Research (2004), 10(11), 3839-3852
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to examine interactions between the proteasome inhibitor bortezomib (Velcade) and the histone deacetylase (HDAC) inhibitors sodium butyrate and suberoylanilide hydroxamic acid in human multiple myeloma (MM) cells that are sensitive and resistant to conventional agents. MM cells were exposed to bortezomib for 6 h before the addition of HDAC inhibitors (total, 26 h), after which reactive oxygen species (ROS), mitochondrial dysfunction, signaling and cell cycle pathways, and apoptosis were monitored. The functional role of ROS generation was assessed using the free radical scavenger N-acetyl-L-cysteine. Preincubation with a subtoxic concentration of bortezomib markedly sensitized U266 and MM.1S cells to sodium butyrate- and suberoylanilide hydroxamic acid-induced mitochondrial dysfunction; caspase 9, 8, and 3 activation; and poly(ADP-ribose) polymerase degradation; resulting in synergistic apoptosis induction. These events were associated with nuclear factor κB inactivation, c-Jun NH2-terminal kinase activation, p53 induction, and caspase-dependent cleavage of p21CIP1, p27KIP1, and Bcl-2, as well as Mcl-1, X-linked inhibitor of apoptosis, and cyclin D1 down-regulation. The bortezomib/HDAC inhibitor regimen markedly induced ROS generation; moreover, apoptosis and c-Jun NH2-terminal kinase activation were attenuated by N-acetyl-L-cysteine. Dexamethasone- or doxorubicin-resistant MM cells failed to exhibit cross-resistance to the bortezomib/HDAC inhibitor regimen, nor did exogenous interleukin 6 or insulin-like growth factor I block apoptosis induced by this drug combination. Finally, bortezomib/HDAC inhibitors induced pronounced lethality in primary CD138+ bone marrow cells from MM patients, but not in the CD138- cell population. Sequential exposure to bortezomib in conjunction with clin. relevant HDAC inhibitors potently induces mitochondrial dysfunction and apoptosis in human MM cells through a ROS-dependent mechanism, suggesting that a strategy combining these agents warrants further investigation in MM.

IT 50-02-2, Dexamethasone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequential exposure to bortezomib combined with clin. relevant NaB, SAHA increased mitochondrial injury, caspase activation, synergistic apoptosis induction in human dexamethasone-sensitive MM.1S cells through ROS-dependent mechanism)
RN 50-02-2 HCAPLUS
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

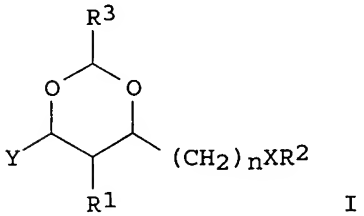


REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 17 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:310834 HCAPLUS
DOCUMENT NUMBER: 140:339332
TITLE: Preparation of trisubstituted dioxanes as histone deacetylase inhibitors.
INVENTOR(S): Schreiber, Stuart L.; Sternson, Scott M.; Wong, Jason C.; Grozinger, Christina M.; Haggarty, Stephen J.; Koeller, Kathryn M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 177 pp., Cont.-in-part of U.S. Pat. Appl. 2003 187,027.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004072849	A1	20040415	US 2003-621276		20030717
US 2003187027	A1	20031002	US 2002-144316		20020509
PRIORITY APPLN. INFO.:			US 2001-289850P	P	20010509
			US 2002-144316	A2	20020509

OTHER SOURCE(S): MARPAT 140:339332
GI



I

AB Title compds. [I; R1, Y = H, aliphatyl, alicyclyl, heteroaliphatyl, heterocyclyl, aryl, heteroaryl; n = 1-5; R2 = R1, protecting group; X = O, S, C(R2a)2, NR2a; R2R2a = atoms to form alicyclyl, heterocyclyl, aryl, heteroaryl; R3 = aliphatyl, alicyclyl, heteroaliphatyl, heterocyclyl, aryl, heteroaryl], were claimed. Thus, rel-N-[4-[(2R,4R,6S)-4-[[(4,5-

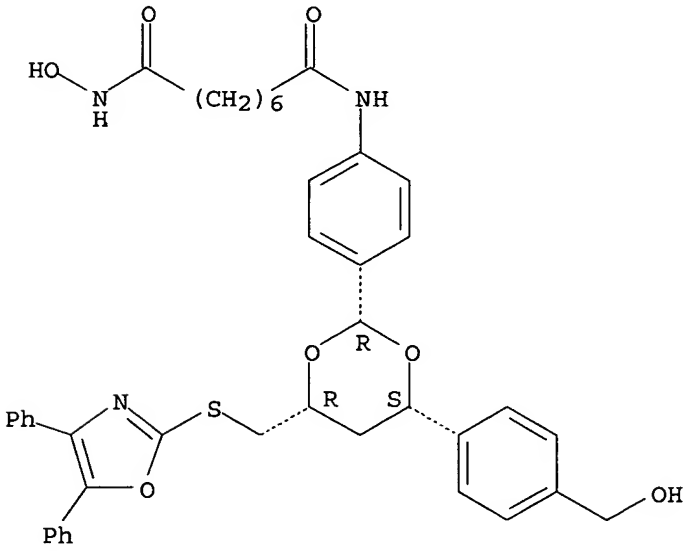
diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-octanediamide (tubacin, claimed compound) at ≥125 nM in A549 cells strongly increased α-tubulin acetylation levels. The present invention addnl. provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p.

IT 537049-40-4P, Tubacin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 537049-40-4 HCAPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

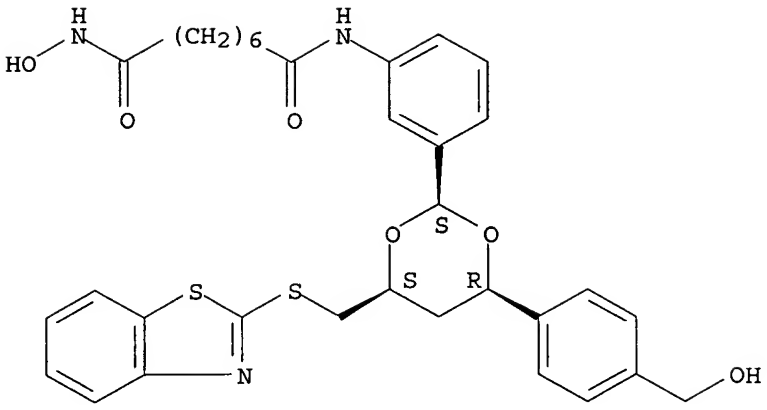


IT 394657-69-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 394657-69-3 HCAPLUS

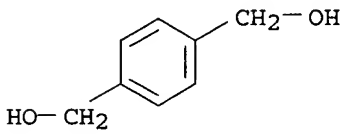
CN Octanediamide, N-[3-[(2R,4R,6S)-4-[(2-benzothiazolylthio)methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

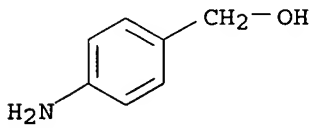


IT 589-29-7, 1,4-Benzenedimethanol 623-04-1, 4-Aminobenzyl alcohol 873-75-6, 4-Bromobenzyl alcohol 1877-77-6, 3-Aminobenzyl alcohol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

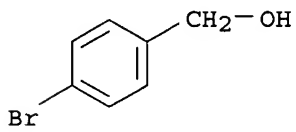
RN 589-29-7 HCAPLUS
CN 1,4-Benzenedimethanol (9CI) (CA INDEX NAME)



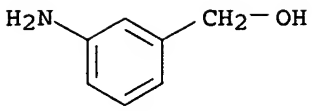
RN 623-04-1 HCAPLUS
CN Benzenemethanol, 4-amino- (9CI) (CA INDEX NAME)



RN 873-75-6 HCAPLUS
CN Benzenemethanol, 4-bromo- (9CI) (CA INDEX NAME)



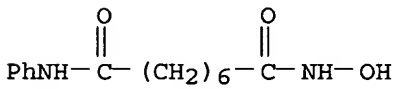
RN 1877-77-6 HCAPLUS
CN Benzenemethanol, 3-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 18 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:51805 HCAPLUS
DOCUMENT NUMBER: 140:263760
TITLE: QSAR Studies of PC-3 cell line inhibition activity of TSA and SAHA-like hydroxamic acids
AUTHOR(S): Wang, Di-Fei; Wiest, Olaf; Helquist, Paul; Lan-Hargest, Hsuan-Yin; Wiech, Norbert L.
CORPORATE SOURCE: Walther Cancer Research Center and Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN, 46556, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 707-711
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quant. structure-activity relationships (QSAR) for a series of new trichostatin A (TSA)-like hydroxamic acids for the inhibition of cell proliferation of the PC-3 cell line have been developed using mol. descriptors from Qikprop and electronic structure calcns. The best regression model shows that the PM3 atomic charge on the carbonyl carbon in the CONHOH moiety(Qco), globularity (Glob), and the hydrophilic component of the solvent-accessible surface area (FISA) describe the IC50 of 19 inhibitors of the PC-3 cell line with activities ranging over five orders of magnitude with an R2=0.92 and F=59.2. This information will be helpful in the further design of novel anticancer drugs for treatment of prostate cancer and other diseases affected by HDAC inhibition.

IT 149647-78-9
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR Studies of PC-3 cell line inhibition activity of TSA and SAHA-like hydroxamic acids)
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

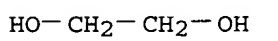
L26 ANSWER 19 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:928863 HCAPLUS
DOCUMENT NUMBER: 140:145869
TITLE: Novel histone deacetylase inhibitors: design, synthesis, enzyme inhibition, and binding mode study of SAHA-based non-hydroxamates
AUTHOR(S): Suzuki, Takayoshi; Nagano, Yuki; Matsuura, Azusa; Kohara, Arihiro; Ninomiya, Shin-Ichi; Kohda, Kohfuku; Miyata, Naoki

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya, Aichi, 467-8603, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(24), 4321-4326
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:145869

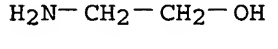
AB In order to find novel non-hydroxamate histone deacetylase (HDAC) inhibitors, a series of compds. modeled after suberoylanilide hydroxamic acid (SAHA) were designed and synthesized as (i) substrate (acetyllysine) analogs, (ii) analogs bearing various functional groups expected to chelate zinc ion, and (iii) analogs bearing nucleophilic functional groups which could bind covalently to HDACs. In this series, PhNHCO(CH2)5NHCONHNH2 and PhNHCO(CH2)nNHCOCH2Br [n = 5, 6] were found to be potent HDAC inhibitors for non-hydroxamates.

IT 107-21-1, Ethylene glycol, reactions 141-43-5, 2-Aminoethanol, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of acylaminoalkanoyl- and carbamoylalkanoylanilines as histone deacetylase inhibitors)

RN 107-21-1 HCAPLUS
CN 1,2-Ethanediol (9CI) (CA INDEX NAME)

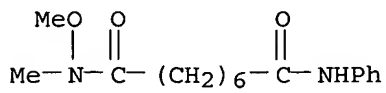


RN 141-43-5 HCAPLUS
CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)



IT 651768-07-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of acylaminoalkanoyl- and carbamoylalkanoylanilines as histone deacetylase inhibitors)

RN 651768-07-9 HCAPLUS
CN Octanediamide, N-methoxy-N-methyl-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 20 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:873334 HCAPLUS
DOCUMENT NUMBER: 139:379965
TITLE: Regulation of microglial inflammatory response by histone deacetylase inhibitors
AUTHOR(S): Suuronen, Tiina; Huuskonen, Jari; Pihlaja, Rea;

Kyrylenko, Sergiy; Salminen, Antero
CORPORATE SOURCE: Department of Neuroscience and Neurology, University of Kuopio, Kuopio, Finland
SOURCE: Journal of Neurochemistry (2003), 87(2), 407-416
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The activation of microglial cells is involved in the pathogenesis of a variety of neurodegenerative diseases, stroke and traumatic brain injuries. Recent studies suggest that protein acetylation can affect the extent of inflammatory responses. The authors' aim was to elucidate whether histone deacetylase inhibitors, inducers of protein hyperacetylation, regulate the inflammatory response in neural models of inflammation in vitro and whether neuron-glia interactions affect this regulation. Interestingly, the authors observed that histone deacetylase inhibitors, such as trichostatin A (TSA) and suberoylanilide hydroxamic acid, strongly potentiated the lipopolysaccharide (LPS)-induced inflammatory response in murine N9 and rat primary microglial cells as well in neural co-cultures and hippocampal slice cultures. TSA clearly potentiated the LPS-induced expression of interleukin (IL)-6 and inducible nitric oxide synthase mRNAs, as well as the secretion of cytokines IL-6, tumor necrosis factor-α and macrophage inflammatory protein (MIP)-2, and nitric oxide (NO). Co-culture and slice culture expts. showed that the presence of astrocytes and neurons did not stimulate or prevent the pro-inflammatory potentiation induced by histone deacetylase inhibitor in microglial cells. The potentiation of cytokine and NO responses was blocked by the nuclear factor kappa B (NF-κB) inhibitors caffeic acid phenethyl ester and helenalin, demonstrating that the NF-κB signaling pathway is involved. The DNA-binding activity of the NF-κB complex was strongly increased by LPS treatment but not enhanced by TSA. This suggests that potentiation of the inflammatory response is not dependent on the level of cytoplasmic NF-κB activation or DNA-binding activity but that site of action may be at the level of transcriptional regulation. The authors' results suggest that environmental stresses, aging, diet and diseases that regulate protein acetylation status may also affect the inflammatory response.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

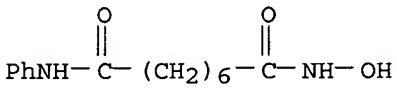
L26 ANSWER 21 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:741697 HCAPLUS
DOCUMENT NUMBER: 140:107316
TITLE: Improved fluorogenic histone deacetylase assay for high-throughput-screening applications
AUTHOR(S): Wegener, Dennis; Hildmann, Christian; Riester, Daniel; Schwienhorst, Andreas
CORPORATE SOURCE: Abteilung fuer Molekulare Genetik und Praeparative Molekularbiologie, Institut fuer Mikrobiologie und Genetik, Goettingen, 37077, Germany
SOURCE: Analytical Biochemistry (2003), 321(2), 202-208
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:107316
AB Histone deacetylases (HDACs) are key targets for chemotherapeutic intervention in malignant diseases. In this paper, a highly sensitive, nonisotopic, homogeneous assay for high-throughput screening of HDAC

inhibitors is presented. The assay is based on a new fluorogenic peptidic substrate of HDACs comprising an ε-acetylated lysyl moiety and an adjacent 4-methylcoumarin-7-amide moiety at the C terminus of the peptide chain. Upon deacetylation of the acetylated lysyl moiety, mols. are recognized as substrates by trypsin, which releases highly fluorescent 7-amino-4-methylcoumarin mols. in a subsequent step of the assay. The fluorescence increase is directly proportional to the amount of deacetylated substrate mols., i.e., HDAC activity. Validation of an improved version of the assay revealed (i) a significantly lower enzyme consumption, (ii) an increased screening window coefficient, (iii) a good tolerance toward organic solvents, and (iv) a good suitability for a whole range of different HDAC-like enzymes. The novel assay thus will expedite studies of HDAC-like enzymes and in vitro screening for drug discovery.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study) (fluorogenic histone deacetylase assay for high-throughput-screening applications)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 22 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:737519 HCAPLUS
DOCUMENT NUMBER: 139:240347
TITLE: Methods of inducing terminal differentiation
INVENTOR(S): Richon, Victoria M.
PATENT ASSIGNEE(S): Aton Pharma, Inc., USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075839	A2	20030918	WO 2003-US6451	20030304
WO 2003075839	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478094	AA	20030918	CA 2003-2478094	20030304
AU 2003213684	A1	20030922	AU 2003-213684	20030304

EP 1487426	A2	20041222	EP 2003-711372		20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003008250	A	20050111	BR 2003-8250		20030304
JP 2005525369	T2	20050825	JP 2003-574115		20030304
CN 1720034	A	20060111	CN 2003-809589		20030304
NO 2004004112	A	20041130	NO 2004-4112		20040928
PRIORITY APPLN. INFO.:			US 2002-361759P	P	20020304
			WO 2003-US6451	W	20030304

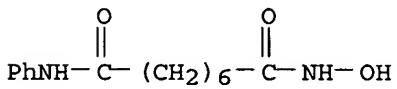
OTHER SOURCE(S): MARPAT 139:240347

AB The present invention provides methods of selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. such as such as suberoylanilide hydroxamic acid (SAHA) in the pharmaceutical compns. of the present invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The present invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo.

IT 149647-78-9P, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of inducing terminal differentiation of neoplastic cells using histone deacetylase inhibitors such as suberoylanilide hydroxamic acid with good bioavailability)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



L26 ANSWER 23 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:379529 HCAPLUS
DOCUMENT NUMBER:	139:345085
TITLE:	Novel biologically based therapies for Waldenstrom's macroglobulinemia
AUTHOR(S):	Mitsiades, Constantine S.; Mitsiades, Nicholas; Richardson, Paul G.; Treon, Steven P.; Anderson, Kenneth C.
CORPORATE SOURCE:	Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE:	Seminars in Oncology (2003), 30(2), 309-312 CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER:	W. B. Saunders Co.
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. Waldenstrom's macroglobulinemia (WM) remains an incurable B-cell malignancy, necessitating urgent development of novel treatment strategies. Building on our experience on bed-to-bedside translational

studies for multiple myeloma (mm), we identified a constellation of novel classes of anti-WM agents, including the proteasome inhibitor PS-341; the ansamycin family of inhibitors (eg, geldanamycin and its analogs) of the heat-shock protein 90 (hsp90) mol. chaperone; histone deacetylase inhibitors, such as suberoylanilide hydroxamic acid (SAHA); and the thiazolidinedione group of peroxisome proliferator-activated receptor-gamma (PPAR-γ) agonists (eg, ciglitazone or rosiglitazone). Our preclin. data show that these classes of agents induce growth arrest and apoptosis of WM cells, at concns. relevant to those achieved in previous clin. uses of these drugs, and suggest that novel therapeutic strategies for WM can be designed to include combinations of these agents, to simultaneously target multiple levels of diverse pathways important for tumor cell growth and survival, and thus maximize the pro-apoptotic activities of these agents and/or neutralize protective responses of WM against their effects. These mol. studies provide a framework for rational design of the next generation of combination therapies for WM.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 24 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:487559 HCAPLUS
DOCUMENT NUMBER: 137:63115
TITLE: Preparation of diphenylazetidinone derivatives as hypolipidemic agents
INVENTOR(S): Glombik, Heiner; Kramer, Werner; Flohr, Stefanie; Frick, Wendelin; Heuer, Hubert; Jaehne, Gerhard; Lindenschmidt, Andreas; Schaefer, Hans-Ludwig
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050068	A1	20020627	WO 2001-EP14532	20011211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10064402	A1	20020627	DE 2000-10064402	20001221
DE 10154520	A1	20031002	DE 2001-10154520	20011107
CA 2431985	AA	20020627	CA 2001-2431985	20011211
AU 2002019173	A5	20020701	AU 2002-19173	20011211
EE 200300237	A	20030815	EE 2003-237	20011211
EP 1345932	A1	20030924	EP 2001-271371	20011211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001016482	A	20040203	BR 2001-16482	20011211
JP 2004516293	T2	20040603	JP 2002-551564	20011211
NZ 526592	A	20041126	NZ 2001-526592	20011211
RU 2275370	C2	20060427	RU 2003-122219	20011211

US 2002128252	A1	20020912	US 2001-21028		20011219
US 6498156	B2	20021224			
ZA 2003004092	A	20040419	ZA 2003-4092		20030527
ZA 2003004095	A	20040419	ZA 2003-4095		20030527
NO 2003002733	A	20030814	NO 2003-2733		20030616
HK 1059936	A1	20060127	HK 2004-102849		20040422
PRIORITY APPLN. INFO.:			DE 2000-10064402	A	20001221
			DE 2001-10154520	A	20011107
			WO 2001-EP14532	W	20011211

OTHER SOURCE(S): MARPAT 137:63115
GI

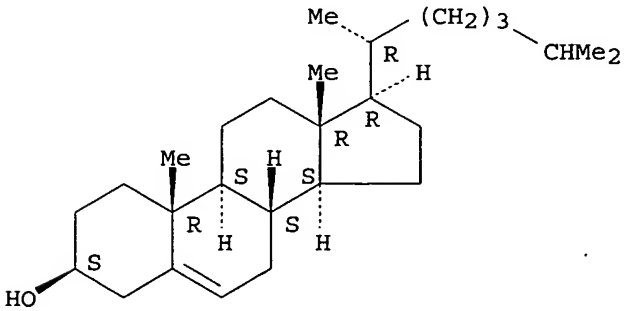
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The compds. are suited for use e.g. as hypolipidemic drugs. The invention discloses preparation of diphenylazetidinone derivs. such as I [R1, R2, R3, R4, R5, R6 = C0-C30-alkylene-L {optionally containing O, CO, CH:CH, C.tplbond.C, N(alkyl), N(alkylphenyl), NH}, H, F, Cl, Br, I, CF3, NO2, CN, CO2H, CO2(alkyl), CONH2, CONH(alkyl), CON(alkyl)2, alkyl, alkenyl, alkynyl, O-alkyl, SO2NH2, SO2NH(alkyl) SO2N(alkyl)2, S-(alkyl), SO(alkyl), (un)substituted S(CH2)nPh, SO(CH2)nPh, SO2(alkyl), SO2(CH2)nPh, NH2, NH(alkyl), N(alkyl)2, NH(acyl), (un)substituted Ph, O(CH2)nPh; n = 0-6; L = II; R7, R9, R10 = Me, Et, Pr, butyl; R8 = H, OH, NH2, NH(alkyl)], and their physiol. acceptable salts, for their use as hypolipidemic agents. Thus, 1,2-diphenylazetidinone derivative III·trifluoroacetate (IV) was prepared via a multistep synthetic sequence starting from 7-[3-(3-butyl-7-dimethylamino-3-ethyl-4-hydroxy-1,1-dioxo-2,3,4,5-tetrahydro-1H-benzo[b]thiepin-5-yl)-phenylcarbamoyl]-heptanoic acid and 4-(4-aminomethylphenyl)-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxyphenyl]-azetidin-2-one. Azetidinone IV was tested for its cholesterol lowering ability [ED50 = 0.01 mg/mouse].

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

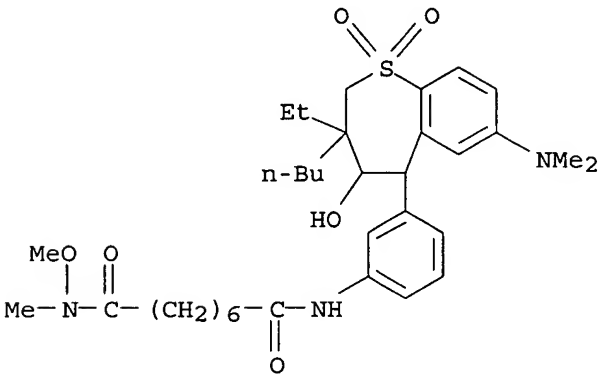
Absolute stereochemistry.



IT 439114-24-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

RN 439114-24-6 HCAPLUS

CN Octanediamide, N'-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 25 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:256222 HCAPLUS
DOCUMENT NUMBER: 136:294651
TITLE: Preparation of aryl-substituted N-hydroxy amides with amide linkages as HDAC inhibitors for treatment of proliferative conditions
INVENTOR(S): Watkins, Clare J.; Romero-Martin, Maria-Rosario; Moore, Kathryn G.; Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza, Einars; Starchenkov, Igor; Dikovska, Klara; Bokaldere, Rasma Melita; Gailite, Vija; Vorona, Maxim; Andrianov, Victor; Lolya, Daina; Semenikhina, Valentina; Amolins, Andris; Harris, C. John; Duffy, James E. S.
PATENT ASSIGNEE(S): Prolifix Limited, UK
SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026696	A1	20020404	WO 2001-GB4329	20010927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2423868	AA	20020404	CA 2001-2423868	20010927
AU 2001090134	A5	20020408	AU 2001-90134	20010927
EP 1335898	A1	20030820	EP 2001-970014	20010927
EP 1335898	B1	20051123		

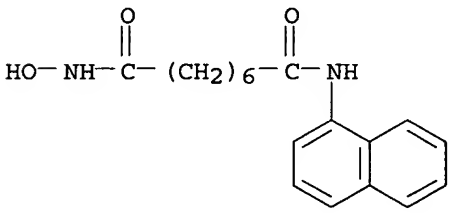
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR						
JP 2004509941	T2	20040402	JP 2002-531082			20010927
EP 1598067	A1	20051123	EP 2005-15737			20010927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR						
AT 310719	E	20051215	AT 2001-970014			20010927
US 2004092598	A1	20040513	US 2003-381791			20030827
PRIORITY APPLN. INFO.:			GB 2000-23985		A	20000929
			US 2001-297785P		P	20010614
			EP 2001-970014		A3	20010927
			WO 2001-GB4329		W	20010927

OTHER SOURCE(S): MARPAT 136:294651

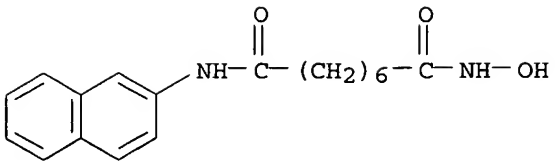
AB The title compds. AQ1JQ2CONHOH [I; wherein A = aryl group; Q1 = aryl leader group having a backbone of at least 2 C atoms; J = NR1CO or CONR1; R1 = amido substituent; Q2 = acid leader group; and pharmaceutically acceptable salts, solvates, amides, esters, ethers, chemical protected forms, and prodrugs thereof] were prepared via solution phase and solid phase synthetic methods as histone deacetylase (HDAC) inhibitors for treatment of proliferative conditions, such as cancer and psoriasis. For example, 6-aminocaproic acid Me ester•HCl was coupled with 2-naphthoyl chloride in the presence of diisopropyl ethylamine in DMF to give the amide. Deesterification (79%), followed by conversion to the N-hydroxyamide using HONH2•HCl in the presence of 1,1'-carbonyldiimidazole in THF, afforded naphthalene-2-carboxylic acid (5-hydroxycarbamoylpentyl)amide II (PX105687) in 40% yield. The latter inhibited recombinant HDAC1 and HDAC2 with IC50 values of 33 nM and 29 nM, resp., and inhibited cell proliferation against the human cervical adenocarcinoma (HeLa) cell line using cell proliferation reagent WST-1 with IC50 of 1.1 nM. Structure-activity relationship studies showed superior activity for I when (1) the backbone of Q1 had > 1 carbon atoms, and (2) the alkylene group Q2 had > 5 carbon atoms.

IT 408357-61-9P, PX 116218 408357-69-7P, PX 116223
408357-72-2P, PX 117720
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HDAC inhibitor; preparation of N-hydroxy amides with amide linkages as HDAC inhibitors for treatment of proliferative conditions)

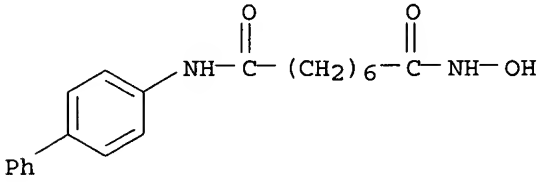
RN 408357-61-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-1-naphthalenyl- (9CI) (CA INDEX NAME)



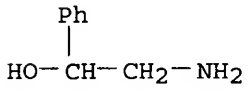
RN 408357-69-7 HCAPLUS
CN Octanediamide, N-hydroxy-N'-2-naphthalenyl- (9CI) (CA INDEX NAME)



RN 408357-72-2 HCAPLUS
CN Octanediamide, N-[1,1'-biphenyl]-4-yl-N'-hydroxy- (9CI) (CA INDEX NAME)



IT 7568-93-6, 2-Amino-1-phenylethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of N-hydroxy amides with amide linkages as HDAC inhibitors for treatment of proliferative conditions)
RN 7568-93-6 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)- (9CI) (CA INDEX NAME)



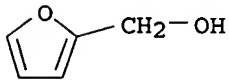
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 26 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:473039 HCAPLUS
DOCUMENT NUMBER: 134:237776
TITLE: A versatile polymer-supported 4-(4-methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis of pseudopeptides. [Erratum to document cited in CA133:223027]
AUTHOR(S): Atkinson, Gail E.; Fischer, Peter M.; Chan, Weng C.
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Journal of Organic Chemistry (2000), 65(16), 5076
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 5052, Compound 21 should be named (Z)-4-phenylbenzoyl dehydroaminobutyric acid.
IT 98-00-0, Furfuryl alcohol 636-72-6, 2-Thiophenemethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis

(Erratum))

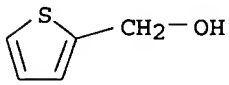
RN 98-00-0 HCAPLUS

CN 2-Furanmethanol (9CI) (CA INDEX NAME)



RN 636-72-6 HCAPLUS

CN 2-Thiophenemethanol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



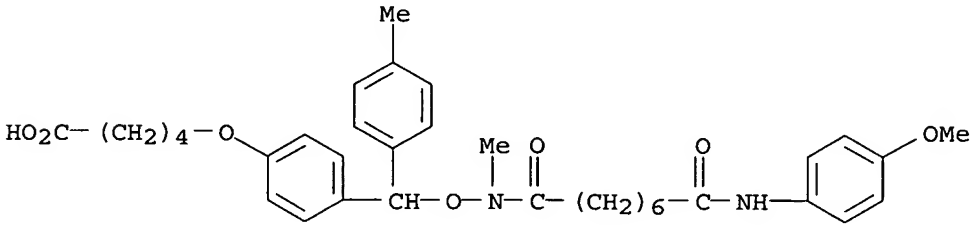
IT 291767-52-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis (Erratum))

RN 291767-52-7 HCAPLUS

CN Pentanoic acid, 5-[4-[[[[8-[(4-methoxyphenyl)amino]-1,8-dioxooctyl]methylamino]oxy](4-methylphenyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)



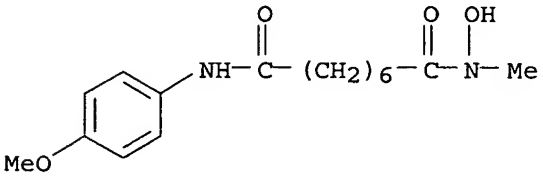
IT 291767-33-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis (Erratum))

RN 291767-33-4 HCAPLUS

CN Octanediamide, N-hydroxy-N'-(4-methoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)

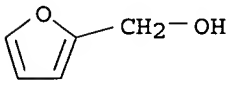


L26 ANSWER 27 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:455849 HCAPLUS
DOCUMENT NUMBER: 133:223027
TITLE: A Versatile Polymer-Supported 4-(4-Methylphenyl(chloro)methyl)phenoxy Linker for Solid-Phase Synthesis of Pseudopeptides
AUTHOR(S): Atkinson, Gail E.; Fischer, Peter M.; Chan, Weng C.
CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Journal of Organic Chemistry (2000), 65(16), 5048-5056
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:223027

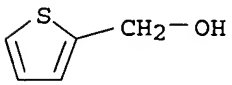
AB The authors reported the preparation and use of benzhydryl chloride linker-resin R-NH-C(O)-(CH2)4-O-4-C6H4-CHCl-4-C6H4-Me [(I); R = resin], for use in solid-phase synthesis of peptides or modified pseudopeptides. Toluene was Friedel-Crafts acylated using 4-methoxybenzoyl chloride, and the methoxy group was cleaved using a solution of boron tribromide in CH2Cl2 to give 4-Hydroxy 4'-methylbenzophenone. O-alkylation with Et 5-bromopentanoate, followed by saponification gave the free acid, which was then coupled to aminomethyl polystyrene to give I, useful as a resin linker in solid-phase syntheses using the Suzuki reaction or standard Fmoc-peptide chemical I was tested for coupling efficiency with N-substituted and N-Fmoc-protected hydroxyamines and amino acids; couplings of 50-88% were found. Quant. release of the coupled amines resulted after treatment with 1% TFA in CH2Cl2 for 75 min at ambient temps. I was used for test prepns. of a N,O-protected nonapeptide, N-acyl-protected amino acid derivs., and peptide alcs. in excellent yields and purities.

IT 98-00-0, Furfuryl alcohol 636-72-6, 2-Thiophenemethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis)

RN 98-00-0 HCAPLUS
CN 2-Furanmethanol (9CI) (CA INDEX NAME)

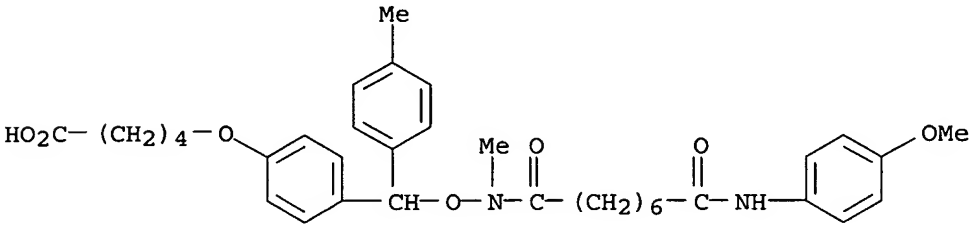


RN 636-72-6 HCAPLUS
CN 2-Thiophenemethanol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

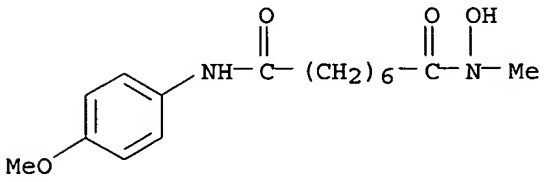


IT 291767-52-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis)

RN 291767-52-7 HCAPLUS
CN Pentanoic acid, 5-[4-[[[[8-[(4-methoxyphenyl)amino]-1,8-dioxooctyl]methylamino]oxy](4-methylphenyl)methyl]phenoxy]- (9CI) (CA INDEX NAME)



IT 291767-33-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and use of versatile polymer-supported (methylphenyl(chloro)methyl)phenoxy linker for solid-phase synthesis)
RN 291767-33-4 HCAPLUS
CN Octanediamide, N-hydroxy-N'-(4-methoxyphenyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 28 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:381950 HCAPLUS
DOCUMENT NUMBER: 131:135225
TITLE: Stability and Structure of Metal Ion Complexes Formed in Solution with Acetyl Phosphate and Acetonylphosphonate: Quantification of Isomeric Equilibria
AUTHOR(S): Sigel, Helmut; Da Costa, Carla P.; Song, Bin; Carloni, Paolo; Gregan, Fridrich
CORPORATE SOURCE: Institute of Inorganic Chemistry, University of Basel, Basel, CH-4056, Switz.
SOURCE: Journal of the American Chemical Society (1999), 121(26), 6248-6257
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The acidity consts. of H2(AcP) and H2(AnP), where AcP2- = acetyl phosphate and AnP2- = acetonylphosphonate, as well as the stability consts. of the 1:1 complexes formed between Mg2+, Ca2+, Sr2+, Ba2+, Mn2+, Co2+, Ni2+, Cu2+, Zn2+, or Cd2+ and AcP2- or AnP2- were determined by potentiometric pH titrns. in aqueous solution (25 °C; I = 0.1 M, NaNO3). On the basis of previously established log KMM(R-PO3) vs. pKH(R-PO3)H straight-line plots for phosph(on)ate ligands (R-PO32-), which allow only a simple -PO32-

coordination (Sigel, H.; et al. Helv. Chim. Acta 1992, 75, 2634), it is concluded that the carbonyl oxygen atom of AcP2- and AnP2- participates in complex formation by giving rise to six-membered chelates for all of the mentioned systems except for Ba(AnP) and Sr(AnP), the stability of which corresponds to a simple -PO32- coordination. The formation degree of the chelates formed by the alkaline earth ions and AcP2- is quite pronounced; it amts., for example, for Mg(AcP) and Ca(AcP) to 41% ± 5% and 48% ± 8%, resp. The corresponding results for Zn(AcP) and Cu(AcP) are 59% ± 6% and 76% ± 4%, resp. The formation degree of the six-membered Cu(AnP) chelate increases in water containing 30% or 50% (volume/volume) 1,4-dioxane. This may also be surmised for the other divalent metal ions under conditions of lower solvent polarity and poorer solvating properties than water. Such conditions exist in active-site cavities of enzymes, and the expected effects are briefly discussed. The indicated measurements with AcP have only become possible after the stabilities of the corresponding M(HPO4) complexes had been determined (Saha, A.; et al. J. Biol. Inorg. Chemical 1996, 1, 231) because AcP always contains some phosphate as an impurity; this phosphate content had to be quantified and its effect was carefully considered in the evaluations of the exptl. data. Here is most probably also the main reason why previously published results regarding the stabilities of the Mg(AcP) and Ca(AcP) complexes vary widely; stability consts. of the other M(AcP) complexes have not been determined previously.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 29 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:703065 HCAPLUS
DOCUMENT NUMBER: 128:17185
TITLE: A model of suspension limiters
AUTHOR(S): Becker, Roger; Goedert, Robert; Clements, Andrew; Whittaker, Thomas, III
CORPORATE SOURCE: University of Dayton Research Institute, University of Dayton, Dayton, OH, 45469-0150, USA
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1997), 3146(Nonlinear Optical Liquids and Power Limiters), 62-71
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A model of the response of a suspension to a short, intense laser pulse is described. In the model the particles act as initiators of the response, which develops in the liquid Back propagation of the active region toward the laser is the dominate feature of the response; it can be used to simplify the description. Novel features of the model are the assertion of the existence of a liquid "plasma", i.e., a high d. of free carriers in the liquid, and the development of the plasma in accordance with the Saha relation. The two aspects of the response are absorption by the liquid plasma and scattering from gas bubbles. The relative role of these mechanisms depends on the particulars of the suspension and the intensity of the laser pulse. A computer code implementing the model is described and the results of simulations are presented. Limiting data and images of irradiated suspensions are compared with the predictions of the model. The images are of emitted and scattered light, as well as of shadowgraphs. The implications of the model for the design of suspension limiters is discussed.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

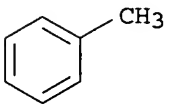
L26 ANSWER 30 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:149209 HCAPLUS
DOCUMENT NUMBER: 124:275855
TITLE: Dielectric relaxation of some disubstituted benzene and aniline derivatives under static and high frequency electric fields
AUTHOR(S): Basak, R. C.; Sit, S. K.; Nandi, N.; Acharyya, S.
CORPORATE SOURCE: Dep. Physics, Univ. Coll., Uttar Dinajpur, 733 134, India
SOURCE: Indian Journal of Physics, B (1996), 70B(1), 37-50
CODEN: IJPBDU; ISSN: 0252-9254
PUBLISHER: Indian Association for the Cultivation of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A convenient method has been suggested for simultaneous determination of relaxation time τj and hence dipole moments μj and μs of some disubstituted benzenes and anilines in solvent benzene and carbon tetrachloride under the effective dispersive region of 9.945 GHz elec. field. The use has been made of the ratio of slopes of the concentration variation of the imaginary part and the real part of the total conductivity Kij* without the prior knowledge of any one of the two (Murthy et al. 1989). The μj and μs thus estimated, are then compared to establish the fact that they are slightly influenced by the high frequency elec. field. The are again compared with the dipole moments μ1 and μ2 (Saha et al. 1994), due to the flexible part and the whole mol. only to show that the probability of rotation of a part of the mol. is possible, under high frequency elec. field.

L26 ANSWER 31 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:620301 HCAPLUS
DOCUMENT NUMBER: 121:220301
TITLE: Quantitative study of the mechanism of ethanol effect in ICP-AES. I. Relative contribution of ethanol interference function and various interference factors
AUTHOR(S): Lu, Hongchun; Zhang, Xulong; Chen, Xinlan
CORPORATE SOURCE: Dep. Chem., Nankai Univ., Tianjin, 300071, Peop. Rep. China
SOURCE: Fenxi Shiyanshi (1993), 12(4), 1-6
CODEN: FENSE4; ISSN: 1000-0720
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of ethanol on different interference elements in ICP-AES has been studied in this paper. By applying Einstein-Boltzmann-Saha equation and Raoult-Clausius-Clapeyron equation, the relative contribution of interfering elements to interference effects (represented by interference factor) has been discussed quant. The expts. show that the changes of Boltzmann factor and activity coefficient are decisive for the enhancement of ethanol. Furthermore, the equation between the concentration of ethanol and the uptake rate, the interference factor (after correcting the uptake rate), the activity coefficient has been obtained.

L26 ANSWER 32 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:449131 HCAPLUS
DOCUMENT NUMBER: 121:49131
TITLE: Quantitative study of the mechanism of ethanol effect in ICP-AES. I. Relative contribution of ethanol interference function and various interference factors
AUTHOR(S): Liu, Hongchun; Zhang, Xuhong; Chen, Xinkun
CORPORATE SOURCE: Dep. Chem., Nankai Univ., Tianjin, 300071, Peop. Rep.

China
SOURCE: Fenxi Shiyanshi (1993), 12(4), 1-6
CODEN: FENSE4; ISSN: 1000-0720
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of ethanol on different interference factors in ICP-AES was studied in this paper. By applying Einstein-Boltzmann-Saha equation and Raoult-Clausius-Clapeyron equation, the relative contribution of interfering factors to interference effects (represented as math. factor) is discussed quant. The expts. show that the changes of Boltzmann factor and activity coefficient contributed for the enhancement of ethanol. Furthermore, an equation for relating concentration of ethanol and the uptake rate, the math. interference factor (after correcting the uptake rate), and activity coefficient was obtained.

L26 ANSWER 33 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:30372 HCAPLUS
DOCUMENT NUMBER: 120:30372
TITLE: Hyperthermal surface ionization of organic molecules
AUTHOR(S): Kishi, Hiroshi; Fujii, Toshihiro
CORPORATE SOURCE: Dep. Chem. Biochem., Oyama Natl. Coll. Technol., Oyama, 323, Japan
SOURCE: Journal of the Mass Spectrometry Society of Japan (1993), 41(1), 51-62
CODEN: JMSJEY; ISSN: 0542-8645
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Hyperthermal surface ionization of toluene and piperidine in seeded supersonic mol. beams was studied. The accelerated mols. were expanded from a nozzle and brought to collision with Ni and ReO2 surfaces. Results were obtained as a function of incident kinetic energy and system parameters, indicating that surface ionization increased drastically above the threshold kinetic energy of 3.5 eV for toluene/Ni and 3.4 eV for piperidine/ReO2. A modified Saha-Langmuir equation of ionization degree was proposed involving kinetic energy, surface property, and surface temperature
IT 108-88-3, Toluene, properties
RL: PRP (Properties)
(hyperthermal ionization of, on nickel surface)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 34 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:661702 HCAPLUS
DOCUMENT NUMBER: 119:261702
TITLE: Analysis of slurries by inductively coupled plasma mass spectrometry using desolvation to improve transport efficiency and atomization efficiency
AUTHOR(S): Hartley, James H. D.; Hill, Steve J.; Ebdon, Les
CORPORATE SOURCE: Plymouth Anal. Chem. Res. Unit, Univ. Plymouth, Plymouth/Devon, PL4 8AA, UK
SOURCE: Spectrochimica Acta, Part B: Atomic Spectroscopy

(1993), 48B(11), 1421-33
CODEN: SAASBH; ISSN: 0584-8547
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A slurry sample introduction system incorporating a heated spray chamber and a condenser, cooled using Peltier coolers, has been designed to desolvate the slurry before entry into the plasma. Drying the slurry increased the transport efficiency (2.2-4.9%) and the atomization efficiency. This enhanced both sensitivities and recoveries. The increase in the recovery enabled larger particles to be fully atomized (≈8 μm c.f. ≈3 μm) principally because of the desolvation that decreases the droplet size of the particles that enter the plasma. Fractionation of the samples before anal. by inductively coupled plasma mass spectrometry, using a cascade impactor, enabled information about the transport efficiency and recoveries to be obtained and also effects of inhomogeneity in the sample to be observed The desolvation of the slurry also caused a decrease in the ionization temperature (from ≈6400° to ≈5500°). Local thermal equilibrium is supposed to be obtained and the ionization temperature here is obtained from the Saha equation. The reason for the increase in the recoveries is therefore considered to be due to the removal of the jacket of aqueous solvent around the particle. The ionization temperature of the plasma can be increased by increasing the forward power or by the addition of mol. gases to the nebulizer gas, particularly hydrogen. The addition of 1.5% volume/volume hydrogen can raise the ionization temperature from about 5500 to 8400°.

L26 ANSWER 35 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:526241 HCAPLUS
DOCUMENT NUMBER: 107:126241
TITLE: Positive ion emission from a platinum hot wire gas sensor
AUTHOR(S): Sears, W. M.; Moen, V. A.; Miremadi, Bijan K.; Frindt, R. F.; Morrison, S. Roy
CORPORATE SOURCE: Fac. Sci., Simon Fraser Univ., Burnaby, BC, V5A 1S6, Can.
SOURCE: Sensors and Actuators (1987), 11(3), 209-20
CODEN: SEACDX; ISSN: 0250-6874
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hot (500° to 1000°) metal wires in contact with organic vapors or contaminated by surface C will emit pos. ions in air. With appropriate bias and collection geometry, currents up to 100 nA can be detected. As the C burns on a contaminated wire and the wire becomes cleaner, the current decays to zero. A clean Pt wire that is a good oxidation catalyst produces a steady pos. ionic current in the presence of organic vapors. A number of different vapors were tested and it was concluded that higher responses were obtained for vapors with higher nos. of C atoms per mol. and greater ease of oxidation by the wire. Oxidizable gases with little or no C produced little or no ionic response. The Saha-Langmuir equation is used to calculate the ionization energies required to emit pos. ions from the surface of the hot metal wire. This gave ionization potentials of about 6 eV, which are too low to represent ionization potentials for C itself or an oxide of C and therefore must represent some, as yet unknown, intermediate of the oxidation reaction. It is concluded that both the clean and C-contaminated wire responses can be used to design selective gas sensors. At 800°, for example, a clean Pt wire works as a highly reproducible gas sensor, giving a linear response from about 10 ppm to 1% vapor concentration of acetone.

L26 ANSWER 36 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:78916 HCAPLUS
DOCUMENT NUMBER: 62:78916
ORIGINAL REFERENCE NO.: 62:13975f-h
TITLE: Ion emission from heated metal surfaces
AUTHOR(S): Lichtman, David
CORPORATE SOURCE: Honeywell Res. Center, Hopkins, MN
SOURCE: J. Vacuum Sci. Technol. (1965), 2(2), 91-2
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pos. ion emission from heated metal targets was observed at <1000°K. during expts. on interaction of beams and surfaces in high vacuum. Data were obtained in a 6-in. radius 60° sector high-vacuum mass spectrometer, cryogenically and ion pumped. The apparatus was of metal construction except for incorporation of sapphire and Kovar glass windows. Electron interaction with surface adsorbed gases gave evidence of release of cleaning solvents. When the target (303 stainless steel) was heated alone, the spectrum of ions leaving the target gave peaks of all the alkalis (Li, Na, K, Rb, and Cs), none of which was intentionally added. The ion current of each species was plotted vs. 1/T (Saha-Langmuir equation), providing linear curves of reproducible slope. Activation energies were 4.50 and 3.42 ev. for Na+ and 3.81 and 3.15 ev. for K+, resp., from 2 303 stainless steel substrates. By using Mo with evaporated Al coating, lower activation energies were determined for Na+ and K+, with Na+ having the larger value. This stable, but variable ion output could be a source of variation in reported results. The use of a low-power-d. electron beam (1 μamp./cm.2 at 100 v.) always resulted in desorption of F and Cl ions. Alkali halide impurities migrate as mols. or clusters of mols. through the vacuum system.

L26 ANSWER 37 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:43379 HCAPLUS
DOCUMENT NUMBER: 62:43379
ORIGINAL REFERENCE NO.: 62:7610a-e
TITLE: Thermal decomposition of nitroacylarylamines
AUTHOR(S): Ruechardt, Christoph; Freudenberg, Bertram
CORPORATE SOURCE: Univ. Munich, Germany
SOURCE: Tetrahedron Letters (1964), (48), 3623-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: German
AB cf. CA 61, 13143d. The thermal decomposition of PhN(NO)COR (I) (R = Me)(II) led by a rate-controlling isomerization to the diazoacetate, PhN:-NOCOR (III) (R = Me) (IV), in equilibrium with the ion-pair PhN+:NO-COR (V) (R = Me) (VI) on the one hand, and decomposing by a rapid side reaction on the other hand into N, Ph, and O2CR radicals. The absence of CO2 evolution was explained through assumption of a cage-reaction, recently refuted (Elid and Saha, CA 61, 11871b). The thermal decomposition of nitrosoacylanilides (whose acyloxy radicals must readily decarboxylate) was investigated in C6H6 at 25° and the data tabulated (R, concentration in mole/l., % N, % CO2, % biphenyl given): Me, 0.100, 90-5, 0.3, 65; PhCH2, 0.100, 80-5, 3.4-6.1, 55-8; PhOCH2, 0.106, 97, 2.8-3.3, 64-72; and EtO2C, 0.085, 71-5, 5.9-6.7, 64-7. Although PhCH2CO2, PhOCH2CO2, and EtO2CCO2 radicals should decarboxylate unmeasurably rapidly, only 0.3-6.7% CO2 was evolved. The decomposition of II (0.099 mole) in C6H6 at 25° in the presence of 0.885 mole/l. acid anhydride (RCO)2O gave the listed yields of CO2 (R and % CO2 given): Me, 1.3-2.9; PhCH2, 20.4-22.4; iso-Pr, 5.2-6.3; and Ph2CH, 24.1. The CO2 yield from I (R = PhCH2) also varied

between 2 and 13% according to concentration and solvent. Accordingly, the main path of decomposition of III was not through the acyloxy radical. Presently proposed mechanisms did not succeed in clarifying the dependence of the decomposition reaction on the solvent or the fact that the kinetics of the reaction were so readily disturbed. A suitable mechanism was proposed. Following the rate-determining 1,3-rearrangement and ionization to VI a chain reaction set in, initiated by the attack of an acetate ion on II: PhN(NO)Ac + AcO- → PhN:NO- (VII) + Ac2O. The diazotate ion (VII) and diazonium ion (VI) then coupled to the diazo anhydride, PhN:NON:NPh, which yielded Ph and PhN:NO (VIII) radicals by the Gomberg reaction. The chain-carrying VII was then reformed from VIII through the intermediate diazo hydroxide, PhN:NOH. This proposed mechanism accounted for lack of CO2 evolution and polymer acetoxy end groups and was in accordance with the exptl. findings. E. S. R. observation of the decomposition of 400 mg. II in 3 ml. C6H6 showed the presence throughout the reaction of an intensive triplet between 3331.0 and 3368.5 oe., of which each line showed hyperfine splitting into at least 14 lines 0.9 oe. apart, as expected from VIII, if the lone electron was located on the N atom of the NO group. The coupling constant, 11.7 oe., was of the expected order of magnitude.

L26 ANSWER 38 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:46167 HCAPLUS
DOCUMENT NUMBER: 56:46167
ORIGINAL REFERENCE NO.: 56:8754a-i,8755a-i,8756a-c
TITLE: Synthesis of cliterpenea. IV. Methyl (±)-deisopropyldehydroabietate
AUTHOR(S): Barltrop, J. A.; Day, A. C.
CORPORATE SOURCE: Univ. Oxford, UK
SOURCE: Tetrahedron (1961), 14, 310-19
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 55, 6521b.--1,2,3,4,9,10,11,12-Octahydro-12-methyl-1-oxophenanthrene (I) was converted to 1-acetyl-1-bromo 1,2,3,4,9,10,11,12-octahydro-12-methylphenanthrene (II), which was converted by Favorskii rearrangement to the title compound (III). Me3COK (from 9.6 g. K) and 10 g. 1-acetylcyclohexene stirred 15 min. (N atmospheric) in 250 ml. dry Me3COH with gentle warming, the solution treated dropwise with 70 g. MeI at 0°, kept 2.5 hrs. at 207deg;, and filtered, KI taken up in H2O, the solution extracted with Et2O, and the combined organic solns. distilled gave 3.7 g. 1-acetyl-1-methyl2-cyclohexene, b10 58-67°, n14D 1.4668; semicarbazone m. 136° (MeOH). Preparation according to Stork and Burgstahler (CA 46, 4519g) gave 3-methyl-2-phenethylcyclohexen-2-one (IV), b0.1 118-20° (b0.1 110-17°, n16D 1.5525; according to Saha, et al. (CA 50, 4084h); 2,4-dinitrophenylhydrazone m. 172°; semicarbazone m. 183-4°. Treatment of IV with H3PO4 at 150-5° and distillation of the product gave I, b0.7 115-20°, n18D 1.5643, λ 266, 273, 290infl. mμ (log ε 2.69, 2.64, 1.74); semicarbazone m. 225-7°. KNH2 (from 44 g. K) and 100 g. 1-methoxy-5-methyl-1,4-cyclohexadiene in 2.5 l. liquid NH3 stirred 20 min. and treated dropwise in 2 hrs. with 100 g. PhCH2CH2Br in 200 ml. dry Et2O, the mixture stirred 2 hrs. before treatment with 100 g. NH4Cl and 2.5 l. H2O, extracted with Et2O, the oil refluxed 2 hrs, with 200 ml. 2N H2SO4, extracted with Et2O, the extract washed with 10% aqueous Na2CO3 and H2O, the dried extracted distilled, and the fraction, b0.05 102-12°, redistd. gave 54 g. oil, b0.3 124-30°, n17D 1.5512; 2,4-dinitrophenylhydrazone m.

172°. The presence of an isomeric impurity was indicated by infrared comparison with authentic IV. The oil treated with H3PO4 at 150-57deg; and twice distilled at 0.05 mm. gave 31 g. oil, n18D 1.5860. A portion (960 mg.) chromatographed on 60 g. Al2O3 and eluted with 350 ml. ligroine gave 360 mg. non-ketonic fraction A. Elution with 200 ml. 1:1 ligroine-C6H6 gave 480 mg. I and further elution with 150 ml. of the same solvent yielded 60 mg. unidentified saturated ketone, inert to alc. NaOEt. Fraction A (2.03 g.) rechromatographed on 100 g. Al2O3 and eluted with 200 ml. petr. ether gave 1.64 g. 1,2,3,4-tetrahydro-3-methylphenanthrene (V), b13 155°, n19D 1.6110, ν 815, 792, 767, 745 cm.-1, λ 229, 274.5, 280, 291, 307.5, 314, 321.5 mμ (log ε 4.99, 3.74, 3.77, 3.67, 3.03, 2.82, 2.96); picrate m. 104.5-5.5 (alc.). Further elution with 100 ml. ligroine gave 198 mg. intermediate fraction and with 300 ml. ligroine 198 mg. 3-methyl-2-phenethylanisole, b13 153°, n18D 1.5636, ν 1255, 1034, 803, 772, 696 cm.-1, λ 275, 280 mμ (log ε 3.41, 3.40). Contaminants in I prepared by the latter method were readily removed during purification of the ethynylation product, 1-ethynyl-1,2,3,4,9,10,11,12-octahydro-1-hydroxy-12-methylphenanthrene (VI). V (1 g.) heated (Natm.) 1 hr. at 300° with 5% Pd-C, the product chromatographed on 50 g. Al2O3, eluted with 100 ml. petr. ether to remove a mixed fraction containing much V, further eluted with 150 ml. solvent, and the fraction (736 mg.) recrystd. 3 times from alc. gave 3-methylphenanthrene (VII), m. 57.5-60.0°, λ 252. 276.5, 284, 295.5, 317.5, 324.5, 332, 340, 347.5 mμ (log ε 4.91, 4.19, 4.06, 4.17, 2.57, 2.52, 2.75, 2.54, 2.81); picrate, m. 137-8, chromatographed from C6H6 on Al2O3 and eluted with C6H6 to give VII, m. 61-2° (alc.). I was extremely unreactive and treatment with HC.tplbond.CLi in liquid NH3 under very vigorous conditions gave VI in only 40% yield. Dry, MeOH-free C2H2 passed through 4.2 g. Li in 500 ml. liquid NH3, the solution and 8.5 g. I in 200 ml. dry tetrahydrofuran saturated 1 hr. at -60° with C2H2 in a 1 l. cooled steel bomb, the sealed bomb shaken 46 hrs. at 20°, cooled to -66°, the mixture extracted with brine and Et2O, the oily product chromatographed on 500 g. deactivated Al2O3 (containing 5% of 10% aqueous AcOH) and eluted with 1.5 l. 9:1 ligroine-C6H6 to give 2.85 g. non-ketonic material, eluted with 2 l. solvent to yield 0.58 g. I and with 0.5 l. solvent to give 0.09 g. mixed fraction, eluted with 3.5 l. 1:1 ligroine-C6H6 and the solvent distilled gave 1.90 g. VI, ν 3521, 3430, 3295 cm.-1 I (12.3 g.) in 200 ml. dry Et2O and 50 g. K in 1050 ml 16:5 Me3COH-Et2O added dropwise in 1.25 hrs. with vigorous stirring at -5 to 0° to 200 ml. dry Et2O saturated with Me2CO-free C2H2, the mixture stirred 24 hrs. at 20° with constant passage of C2H2 and diluted with 500 ml. brine before acidification with concentrated HCl and extraction with Et2O, the dark oily product taken up in 200 ml. 95% alc. and treated with 50 ml. 5% AgNO3 in 95% alc., and the Ag derivative (3.1 g.) refluxed 2.5 hrs. with 15 g. NaCN in 160 ml. 15:1 H2O-alc. and extracted with Et2O gave 1.25 g. VI. VI (1.71 g.) refluxed 2.5 hrs. with 50 ml. 90% HCO2H and 5 ml. alc., the mixture poured into 10% aqueous Na2CO3 and extracted with Et2O, and the viscous residue (1.66 g.) on evaporation chromatographed on 300 g. deactivated Al2O3 and eluted with 700 ml. ligroine gave 60 mg. oil, ν 3290, 2110 cm.-1 Further elutions with 700 ml. and 1400 ml. yielded 440 mg. mixed fractions and 637 mg. unsatd. ketone, 1-acetyl-3,4,9,10,11,12-hexahydro-12-methylphenanthrene (VIII), b0.04 108-11°, n17D 1.5740, λ 216, 234 mμ (log ε 4.03, 3.94); 2,4-dinitrophenylhydrazone m. 209-13° (alc.-EtOAc). Rechromatography of the mixed fractions gave 74 mg.

unidentified oil, ν 1717 cm.-1 and 250 mg. VIII. VIII was obtained in 8% yield by rearrangement of VI in C6H6 with P2O5. Chemical proof of the position of the ethylenic bond in VIII was obtained by degradation. VIII (23 mg.) and 35 mg. OsO4 in 3 ml. dry Et2O and 0.1 ml. dry C5H5N boiled 1 hr. and kept 16 hrs. at 20°, the reagents evaporated at 100° in vacuo and the residue refluxed 30 min. with 200 mg. LiAlH4 in 5 ml. pure tetrahydrofuran, excess LiAlH4 decomposed with EtOAc, the mixture diluted with H2O and extracted with CHCl3, and the extract evaporated gave 24 mg. product, ν 3390, 1709 cm.-1, treated 12 hrs. at 20° with 100 mg. Pb(OAc)4 in 4 ml. AcOH, evaporated at 100°/0.05 mm., diluted with H2O, and extracted with Et2O to give 29 mg. product, giving a pos. Schiff test. The product (19 mg.) in 1.5 ml. Et2O esterified with ethereal CH2N2, chromatographed on 3 g. deactivated Al2O3 and eluted with 15 ml. Et2O gave the aldehydo-ester (IX), ν 2857, 1739 cm.-1, giving a pos. Schiff test (not shown by the dioxane used as solvent). In spite of the failure of the projected stereospecific synthesis at this stage it was of interest to study the alkylation of VIII. VIII (190 mg.) refluxed 30 min. in 2 ml. alc. with 0.08 ml. BzH and 25 mg. KOH, the solution diluted with H2O, acidified, and extracted with Et2O, the extract washed (aqueous NaHSO3, H2O), and the dried solution evaporated, the residue chromatographed on 25 g. Al2O3, and eluted with 4:1 ligroine-C6H6 gave 1-cinnamoyl-3,4,9,10,11,12-hexahydro-12-methylphenanthrene, λ 227, 297 mμ (log ε 4.03. 4.20). VIII (320 mg.), 8 ml. MeI, and 16 ml. 0.8M Me3CCH2ONa in C6H6 kept (N atmospheric) 1.5 hrs. at 20°, the diluted mixture acidified, extracted with Et2O, chromatographed on 20 g. deactivated Al2O3, eluted with 9:1 ligroine-C6H6, and the fraction (140 mg.) distilled gave an α,β-unsatd. ketone, b0.05 115°, λ 229 mμ (E1%1cm. 209), also prepared by use of Me3COK in Me3COH as the basic reagent. The ketone was unaffected by treatment with BzH in alc. KOH. The Favorskii rearrangement was expected to establish the stereochemistry of VIII. VIII (368 mg.) in 10 ml. Et2O and 25 ml. liquid NH3 swirled 15 min. with addition of 110 mg. Na and the blue color eliminated by addition of NH4Cl, the diluted solution extracted with Et2O, the oily product (368 mg., ν 3448, 1700 cm.-1) treated in 2 ml. AcOH with 5.2 ml. 2% CrO3-AcOH 1 hr. at 20°, diluted with H2O, extracted with Et2O, and the product chromatographed on 30 g. Al2O3 and eluted with 400 ml. 1:1 ligroine-C6H6 gave 1-acetyl-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (IXa), b0.15 107°. (IXa) (240 mg.) and 600 mg. p-MeC6H4SO3H in 20 ml. redistd. Ac2O slowly distilled 2.5 hrs. with constant replacement of distilled Ac2O, the Ac2O removed finally at 100°/12 mm., the residue taken up in Et2O, and the solution washed with ice-cold 5% NaOH and H2O, dried, and evaporated gave 290 mg. enol acetate (X), ν 1750, 1208 cm.-1 X (332 mg.) in 10 ml. Me3COH and 220 mg. (CH2CO)2NBr in 20 ml. Me3COH and 11 ml. N H2SO4 mixed and kept 3 hrs. in the dark at 20°, the solution treated with saturated aqueous NaHSO3 diluted with H2O, extracted with Et2O, and the washed (5% aqueous NaOH, H2O) and dried extract evaporated gave 300 mg., II ν 1700, 1351 cm.-1 II (300 mg.) refluxed 6 hrs. in 30 ml. MeOH containing 1 g. Na, the solvents evaporated, the residue diluted with H2O and Et2O, the organic material separated into 195 mg. neutral and 49 mg. acid fractions, the latter methylated, and the combined neutral products (238 mg.) chromatographed on 50 g. deactivated Al2O3 and eluted with 350 ml. ligroine, 100 ml. 19:1 ligroine-C6H6, 150 ml. 19:1 ligroine-C6H6, and stronger solvents gave 98 mg. oils, ν

1727, 1245 cm.-1, 10 mg. mixed fraction, 29 mg. IXa, and 33 mg. oily material. The ester-containing fractions (108 mg.) rechromatographed on 10 g. Al2O3, eluted with 170 ml. 4:1 ligroine-C6H6, the oily semi-solid fraction (52 mg.) twice recrystd. from petr. ether, percolated in ligroine through C, and recrystd. from petr. ether gave 6.3 mg. III, m. 114-15°. Further elution with 1:2 ligroine-C6H6 gave 5 mg. IXa. III (4.0 mg.) was refluxed 5 hrs. with 5 ml. solution (5 g. KOH in 18 ml. 1:5 H2O-HOCH2CH2OH boiled until the temperature rose to 150°) and the diluted solution treated with Et2O and separated into 6.1 mg. neutral and 9.3 mg. acidic fractions, neither of which was obtained crystalline Ghatak's (±)-deisopropyldehydroabietic acid (0.25 mg., CA 54, 15432a) in 0.1 ml. pure tetrahydrofuran esterified with excess ethereal CH2N2, the solvent and reagent evaporated in vacuo, and the product sublimed at 93°/0.05 mm. gave III. Since the trans ester, III, was obtained in only 3% yield from II, it was considered unjustifiable to conclude that the unsatd. ketone VIII had a trans ring junction.

L26 ANSWER 39 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:77730 HCAPLUS
DOCUMENT NUMBER: 53:77730
ORIGINAL REFERENCE NO.: 53:14070b-i
TITLE: Stereochemistry of deoxypodocarpic acid isomers
AUTHOR(S): Ghatak, Usha Ranjan
CORPORATE SOURCE: Indian Assoc. Cultivation Sci., Calcutta
SOURCE: Tetrahedron Letters (1959), 1, 19-23
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Following assignment of definite stereochemistry to cis-deisopropyldehydroabietic acid (I), m. 146-7°, by Saha, et al. (C.A. 50, 11988i), the stereochem. behavior of the racemates, m. 232-3° (II), 205-7° (III), and 186-7° (IV) was investigated. Conjugate addition of HCN to 2-phenethyl-3-methyl-2-cyclohexenone followed by alkaline hydrolysis and esterification gave a good yield of 3-carbomethoxy-3-methyl-2-phenethylcyclohexanone (V), m. 163°. The carbinol formed by treatment of V with MeMgI dehydrated with anhydrous (CO2H)2 in PhMe gave a complex liquid mixture, b0.15 150-60°, λ 5.67, 5.77, 2.86 μ, cyclized by heating 1.5 hrs. on a steam bath with polyphosphoric acid to give liquid neutral material (VI) and a crystalline acidic product, recrystd. (EtOAc-alc .) to give authentic II, C17H22O2; Me ester (VII), m. 131-2° (Haworth and Barker, C.A. 33, 93179). Working up the mother liquor gave the isomeric acid III, C17H22O2, m. 206-7°; Me ester (VIII) m. 84-5°. II and III tend to form a eutectic, m. 190-2°, and on dehydrogenation with 10% Pd-C gave 1-methylphenanthrene. Hydrolysis of VI with 10% KOH in BuOH gave III together with an unidentified low-melting product. The nonhydrolyzed residue yielded VII. VII treated with AcCl in the presence of AlCl3 in PhNO2 and the ketonic product isolated through the semicarbazone gave 6-acetyl-1,4a-dimethyl-1-carbomethoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IX), C20H26O3, m. 133-4° (MeOH), λ 259 mμ (log ε 4.17, alc.); 2,4-dinitrophenylhydrazone m. 234-5°. IX oxidized with BzO2H in CHCl3 yielded DL-Me podocarpate acetate, m. 125-6°, hydrolyzed with alc. KOH to DL-Me podocarpate, m. 193°, converted by hydrolysis with 10% KOH in (HOCH2)2 to DL-podocarpic acid, m. 266-8° (EtOAc-petr. ether) (King, et al., C.A. 50, 14653a). VII oxidized with CrO3 in AcOH afforded 1-carbomethoxy-1,4a-dimethyl-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene, crystallized (MeOH) to give 2 polymorphic forms, m. 124-5°, λ 249 mμ (log ε

4.07, alc.), and m. 146-7°; 2,4-dinitrophenylhydrazone m. 219-20°. Similar oxidation of VIII yielded 1-carbomethoxy-1,4a-dimethyl-9,10-dioxo-1,2,3,4,4a,9, 10,10a-octahydrophenanthrene, m. 129-30°, λ 288 mμ (log ε 3.87, alc.), converted by refluxing with Ac2O and fused NaOAc to the corresponding enol acetate, λ 259 mμ (log ε 4.04), reduced in AcOH containing a drop of 60% HClO4 with 10% Pd-C to VII. The formation of the mono- and dioxo esters on oxidation (Wenkert and Jackson, C.A. 52, 10967i) and the subsequent transformation through the enol acetate proved that the epimeric centers at C-1 are identical in both acids which differ only at ring-junction, II being trans-deoxypodocarpic acid and III, cis-deoxypodocarpic acid. The remaining isomer, deisopropyldehydroabietic acid remains to be described since IV, derived from the 10-oxo acid, is unlikely to have this stereochemistry because of the improbability of epimerization at C-1 through Wolff-Kishner reduction. The possibility that IV may be a eutectic is not entirely ruled out and is under investigation.

L26 ANSWER 40 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:44951 HCAPLUS
DOCUMENT NUMBER: 53:44951
ORIGINAL REFERENCE NO.: 53:8050i,8051a-e
TITLE: Formylation of phenols and phenol ethers by dimethyl-formamide. I
AUTHOR(S): Mangoni, Lorenzo
CORPORATE SOURCE: Univ. Rome
SOURCE: Annali di Chimica (Rome, Italy) (1958), 48, 930-9
CODEN: ANCRAI; ISSN: 0003-4592
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Resorcinol (I) and its ethers react with HCONMe2 (II)-POCl3 (III) with evolution of HCl and formation of a crystalline intermediate, [Me2NC+HAr]PO2Cl2- (IV) (the cation is a resonance hybrid of 4 structures with charge on N, C, or either O). This is hydrolyzed quantitatively to ArCHO, Me2NH, H3PO4, and HCl, and reduced to ArCH2NMe2. [Me2NCHOPOCl2] Cl is thought to be an intermediate. I (22 g.) and 16 cc. II is treated dropwise with 18 cc. III at 50-60°, heated a few min. at 100°, kept overnight, the solid added gradually to 20 g. Na2CO3 in 200 cc. H2O and heated to hydrolyze it (final pH 4-5), then cooled in a freezing mixture to precipitate 19 g. 2,4-(HO)2C6H3CHO, m. 133-4°. Similarly 2.66 g. m-C6H4(OMe)2 gives 2.35 g. 2,4-(MeO)2C6H3CHO, m. 67-8° (2,4-dinitrophenylhydrazone, m. 248-9°); 2.5 g. m-MeOC6H4OH gives 12% 2,4-(MeO)(HO)C6H3CHO, m. 157-8° (best isolated as the dinitrophenylhydrazone in 24% yield, m. 274-5°). II (1.6 cc.) and 1.8 cc. III is treated with cooling with 2.2 g. I, kept overnight, added gradually to 15 cc. chilled (nearly frozen) AcOH, stirred well, filtered, and the precipitate washed with AcOH and Et2O to leave 3.1 g. IV, m. 156-8°. Use of 3.6 g. III gives 4.3 g. IV. IV is soluble in cold H2O, decomposed in hot H2O, insol. in organic solvents, but can be crystallized with care from AcOH. It decompose rapidly in warm NaHCO3 with evolution of Me2NH. IV (2 g.) is hydrogenated in AcOH over 1 g. Pd-C during 7 hrs., the filtered solution evaporated below 50°, the residue dissolved in H2O, made acid, extracted with Et2O, the aqueous layer made alkaline, and extracted continuously with a large volume of Et2O to isolate 1.05 g. 2,4-(HO)2C6H3CH2NMe2 (V) as a glass, chromatographically pure, rather unstable. V picrate m. 105-7°. V is also synthesized. 2,4-(MeOCO2)2C6H3CHO (VI), prepared according to Mitter and Saha (C.A. 28, 5069) m. 97-8°; phenylhydrazone, m. 113-14°;

semicarbazone, m. 172-3° (previously reported as 72°, 138°, and 185°, resp.). VI is oxidized by KMnO4-Me2CO to 2,4-(MeOCO2)2C6H3CO2H, which with POCl3 gives 2,4-(MeOCO2)2C6H3COCl. This reacts with Me2NH in C6H6 at room temperature to give 2,4-(MeOCO2)2C6H3CONMe2, m. 186-7°. This (0.5 g.) is extracted during 18 hrs. from a Soxhlet thimble into 0.5 g. LiAlH4 in 150 cc. Et2O, the excess LiAlH4 decomposed by H2O, the mixture made acid, extracted with Et2O, the aqueous layer made alkaline, filtered, and continuously extracted with Et2O to give V.

L26 ANSWER 41 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1954:17371 HCAPLUS
DOCUMENT NUMBER: 48:17371
ORIGINAL REFERENCE NO.: 48:3136f-h
TITLE: Electron density and temperature in the column of the high-current carbon arc
AUTHOR(S): Maeker, H.
CORPORATE SOURCE: Siemens-Schuckert Werke, Erlangen, Germany
SOURCE: Zeitschrift fuer Physik (1953), 136, 119-36
CODEN: ZEPYAA; ISSN: 0044-3328
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Electron d. and temperature were determined spectroscopically; the former was derived from the Stark-effect widening of the H line, the latter from the electron d. by way of the Saha equation and from the intensity ratio of C lines whose transition probabilities had previously been measured with an alc.-stabilized arc. At a current of 200 amp. a temperature of 10900°K. was determined for a point along the axis at a distance of 1.42 cm. from the cathode. The radial temperature gradient was determined from intensity measurements of O, H, C, and Hg lines. From absolute intensities of certain C lines the C content of the arc was estimated as 30% and the effective ionization potential as 12.25 e.v.

L26 ANSWER 42 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1947:23478 HCAPLUS
DOCUMENT NUMBER: 41:23478
ORIGINAL REFERENCE NO.: 41:4688a-c
TITLE: Studies in glass systems. Magnetic susceptibility of polar crystals dissolved in borax glass
AUTHOR(S): Majumdar, Subodh Kumar; Banerjee, Rama Prasad
CORPORATE SOURCE: Presidency Coll., Calcutta
SOURCE: Indian Journal of Physics (1946), 20, 218-25
CODEN: IJPYAS; ISSN: 0019-5480
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 41, 1912i. The present paper is an extension of the work by Majumdar and Saha (C.A. 40, 2365.4). Measurements were made by means of a torsion balance rather than a Guoy balance as was previously used. Alkali salts such as NaCl, Li2SO4, Na2SO4, and K2SO4 were dissolved in fused borax and the diamagnetic susceptibilities determined The values thus obtained (χM + 106 = -29.17, -41.77, -47.87, -70.22, resp.) are much larger than those for the pure salt; this indicates an expansion of the lattice. This conclusion is counter to that drawn from previous measurements of mole refraction and x-ray diffraction.

L26 ANSWER 43 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1936:47938 HCAPLUS

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L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SAHA/CN
L2               STR
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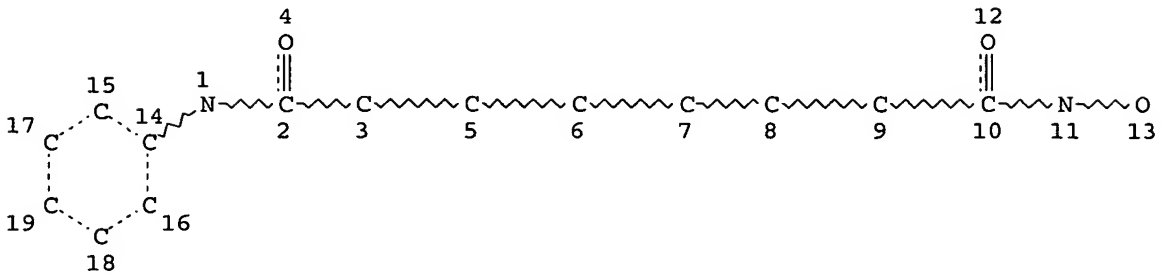


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L4           181 SEA FILE=REGISTRY SSS FUL L2
L5           180 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 NOT L1
L6               SEL  PLU=ON  L1 1- CHEM :        4 TERMS
L7          1403 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6
L8            46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L9        284865 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("X-RAY DIFFRACTION"/CV OR
                 "KOSSEL EFFECT"/CV OR XRD/CV) OR X(W)RAY(W)DIFFRACTION
L11        33989 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALCOHOL/BI
L12         1280 SEA FILE=REGISTRY ABB=ON  PLU=ON  SOLVENT/BI
L13            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHANOL/CN OR ETHANOL/CN OR
                 ISOPROPANOL/CN
L14          411 SEA FILE=REGISTRY ABB=ON  PLU=ON  GELATIN/BI
L15              SEL  PLU=ON  L13 1- CHEM :       89 TERMS
L16      1231961 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15
L17      1925635 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR L11 OR ALCOHOL OR
                 METHANOL OR ETHANOL OR ISOPROPANOL OR ISO(W)PROPANOL
L18       176616 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR GELATIN
L19       963610 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR SOLVENT
L20            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L9
L22            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L18
L23           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L19
L24           12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND (L9 OR L17 OR L18 OR
                 L19)
L25           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)L17
L26           44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 OR L22 OR L23 OR L24 OR
                 L25
L27      1727804 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
                 INJECTIONS, I.V."+ALL/CV OR ?INTRAVEN? OR ?DRUG? OR ?THERAP?
                 OR ?MEDIC? OR ?PHARMA? OR DRUG DELIVERY?/CV
L29          156 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L7 OR L8)(L)L27) NOT L26
L30            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND ?INTRAVE?


=> d ibib abs hitstr l30 1-2

L30  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:82439  HCAPLUS
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DOCUMENT NUMBER: 30:47938
ORIGINAL REFERENCE NO.: 30:6368i,6369a-d
TITLE: Isoflavone series
AUTHOR(S): Mitter, P. C.; Maitra, S. S.
SOURCE: J. Indian Chem. Soc. (1936), 13, 236-9
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The possibility of an isoflavone structure for cyanomaclurin led to an attempt to synthesize the isoflavone, C15H10O6. The preparation of β-resorcylaldehyde di-Me ether (I) (cf. Mitter and Saha, C. A. 28, 5069.4) was improved by decomposing the imino chloride with ice and then with small quantities of ice-cold HCl. An intimate mixture of 16 g. I, 17.5 g. BzNHCH2CO2H and 8 g. fused AcONa was heated with 30 cc. Ac2O for 1 hr., yielding 17.5 g. of the azlactone of I, C18H15NO4, m. 168°, which was hydrolyzed by refluxing for 4 hrs. with 10% NaOH and subsequent saturation with SO2 into 2,4-dimethoxyphenylpyruvic acid, C11H12O5, m. 156°; oxime, m. 145° (decomposition). A mixture of 10 g. of the oxime with 6 cc. Ac2O was heated at 100° and the reaction mixture was shaken with 50 cc. H2O. An oil separated and solidified, yielding 6 g. of 2,4-dimethoxyphenylacetonitrile (II), C10H11NO2, m. 76°. Dry HCl was passed into an ice-cold Et2O solution of 2 g. II and 2 g. phloroglucinol containing 0.8 g. anhydrous ZnCl2. Reddish orange crystals separated overnight and, on recrystn. from H2O, gave 2',4'-dimethoxyphenyl-2,4,6-trihydroxyacetophenone (III), C16H16O6, m. 175°; dibenzyl derivative, C30H28O6, m. 135°. On failure of all attempts at condensation with HCO2Et in the presence of mol. Na (cf. Spath and Lederer, C. A. 24, 3510) a mixture of 1 g. of III and 1 g. fused NaOAc was refluxed with 10 cc. Ac2O at 175-80° for 12 hrs. Treatment of the cold reaction product yielded colorless crystals of 5,7-diacetoxy-2',4'-dimethoxy-2-methylisoflavin, C22H20O8, m. 204-5°, hydrolyzed by 1% alc. KOH and subsequent acidulation to 5,7-dihydroxy-2',4'-dimethoxy-2-methylisoflavone, C18H16O6, m. 213-4°, which gave with FeCl3 a transient violet color changing to dark brown. On warming with dilute NaOH no blue color was produced.

L26 ANSWER 44 OF 44 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1932:3764 HCAPLUS
DOCUMENT NUMBER: 26:3764
ORIGINAL REFERENCE NO.: 26:436e-f
TITLE: Action of o-phthalyl chloride on phenyl and thiophenyl acetates
AUTHOR(S): Knapp, Walter
SOURCE: Monatshefte fuer Chemie (1931), 58, 176-82
CODEN: MOCMB7; ISSN: 0026-9247
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Chakravarti and Saha (C. A. 21, 3192) obtained a compound, m. 101°, from the interaction of o-C6H4(COCl)2 and PhSH, which they considered an isomer of o-C6H4(COSPh)2 but did not explain its formation. K. obtains the same compound by the use of PhSAc and AlCl3 in CS2 and considers it to be the unsym. dithio phenyl ester of o-C6H4(CO2H)2; concentrated H2SO4 gives a light yellow color, changing to light violet on warming: alc. KOH gives the acid and PhSH; oxidation with KMnO4 gives 2 compds., m. 105-6° and 142-4°, which were not identified. PhOAc, o-C6H4(COCl)2 and AlCl3 give o-C6H4(CO2Ph)2.

=> d stat que l30

DOCUMENT NUMBER: 144:403895
TITLE: Clinical experience with intravenous and oral formulations of the novel histone deacetylase inhibitor suberoylanilide hydroxamic acid in patients with advanced hematologic malignancies
AUTHOR(S): O'Connor, Owen A.; Heaney, Mark L.; Schwartz, Lawrence; Richardson, Stacie; Willim, Robert; MacGregor-Cortelli, Barbara; Curly, Tracey; Moskowitz, Craig; Portlock, Carol; Horwitz, Steven; Zelenetz, Andrew D.; Frankel, Stanley; Richon, Victoria; Marks, Paul; Kelly, William K.
CORPORATE SOURCE: Department of Medicine, Division of Hematologic Oncology, Lymphoma Service, Leukemia Service, Division of Solid Tumor Oncology, Developmental Chemotherapy Service, Genitourinary Oncology Service, Department of Radiology, Department of Nursing, Cell Biology Program, Mem. Sloan-Kettering Cancer Center, Sloan-Kettering Institute, New York, NY, USA
SOURCE: Journal of Clinical Oncology (2006), 24(1), 166-173
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To document the toxicity and activity of the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) in patients with pretreated hematol. malignancies. Patients and Methods: Two formulations of SAHA (i.v. [IV] and oral) have been assessed in two consecutive phase I trials. In both trials, dose escalation was performed in parallel and independently in patients with solid tumors and hematol. malignancies. Eligible patients were required to have adequate hepatic and renal function, an absolute neutrophil count ≥ 500/μL and a platelet count more than 25,000/mL. All patients provided informed consent for study inclusion. Results: A total of 39 patients with hematol. malignancy were enrolled (14 on IV SAHA and 25 on oral SAHA), of whom 35 were treated. The spectrum of diseases included patients with diffuse large B-cell lymphoma (n = 12), Hodgkin's disease (HD; n = 12), multiple myeloma (n = 2), T-cell lymphoma (n = 3), mantle cell lymphoma (n = 2), small lymphocytic lymphoma (n = 2), and myeloid leukemia (n = 2). Major adverse events with the oral formulation included fatigue, diarrhea, anorexia, and dehydration, whereas myelosuppression and thrombocytopenia were more prominent with the IV formulation. Typically, the hematol. toxicities resolved shortly after SAHA was stopped. There was no neutropenic fever or neutropenic sepsis. Reduction in measurable tumor was observed in five patients. One patient with transformed small lymphocytic lymphoma met criteria for complete response, whereas another met the criteria for partial response (PR). One patient with refractory HD had a PR, whereas three patients had stable disease for up to 9 mo. Conclusion: These results suggest that SAHA has activity in hematol. malignancies including HD and select subtypes of non-Hodgkin's lymphoma.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:847686 HCAPLUS
DOCUMENT NUMBER: 139:358271
TITLE: Phase I clinical trial of histone deacetylase inhibitor: suberoylanilide hydroxamic acid administered intravenously

AUTHOR(S): Kelly, Wm. Kevin; Richon, Victoria M.; O'Connor, Owen; Curley, Tracy; MacGregor-Curtelli, Barbara; Tong, William; Klang, Mark; Schwartz, Lawrence; Richardson, Stacie; Rosa, Eddie; Drobnjak, Marija; Cordon-Cordo, Carlos; Chiao, Judy H.; Rifkind, Richard; Marks, Paul A.; Scher, Howard

CORPORATE SOURCE: Genitourinary Oncology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center and Joan and Sanford Weill Medical College of Cornell University, New York, NY, 10021, USA

SOURCE: Clinical Cancer Research (2003), 9(10, Pt. 1), 3578-3588
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

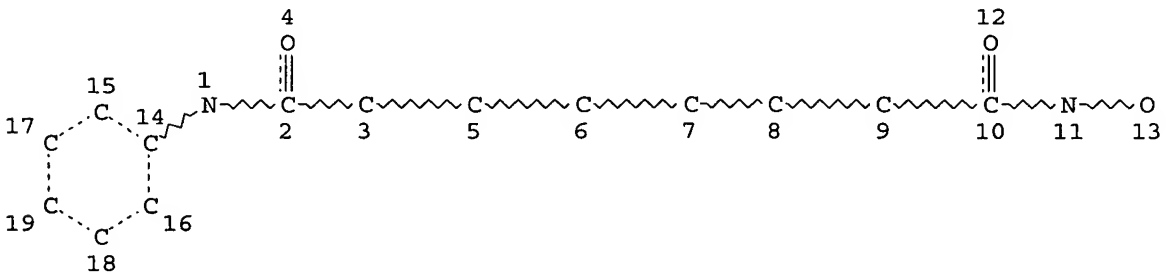
DOCUMENT TYPE: Journal

LANGUAGE: English

AB To evaluate the safety, pharmacokinetics, and biol. activity of suberoylanilide hydroxamic acid (SAHA) administered by 2-h i.v. infusion in patients with advanced cancer. SAHA was administered for 3 days every 21 days in part A and 5 days for 1-3 wk in part B. Dose escalation proceeded independently in patients with solid tumor and hematol. malignancies (part B only). Pharmacokinetic studies were performed along with assessment of acetylated histones in peripheral blood mononuclear cells and tumor tissues. No dose-limiting toxicities were observed in 8 patients enrolled in part A (75, 150, 300, 600, and 900 mg/m2/day). Among 12 hematol. and 17 solid tumor patients enrolled in part B (300, 600, and 900 mg/m2/day), therapy was delayed ≥1 wk for grade 3/4 leukopenia and/or thrombocytopenia in 2 of 5 hematol. patients at 600 mg/m2/day + 5 days for 3 wk. The maximal-tolerated dose was 300 mg/m2/day + 5 days for 3 wk for hematol. patients. One solid patient on 900 mg/m2/day + 5 days for 3 wk developed acute respiratory distress and grade 3 hypotension. The cohort was expanded to 6 patients, and no addnl. dose-limiting toxicities were observed Mean terminal half-life ranged from 21 to 58 min, and there, was dose-proportional increase in area under the curve. An accumulation of acetylated histones in peripheral blood mononuclear cells up to 4 h postinfusion was observed at higher dose levels. Posttherapy tumor biopsies showed an accumulation of acetylated histones by immunohistochem. Four (2 lymphoma and 2 bladder) patients had objective tumor regression with clin. improvement in tumor related symptoms. Daily i.v. SAHA is well tolerated, inhibits the biol. target in vivo, and has antitumor activity in solid and hematol. tumors.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que l32
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SAHA/CN
L2 STR



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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L4           181 SEA FILE=REGISTRY SSS FUL L2
L5           180 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 NOT L1
L6               SEL  PLU=ON  L1 1- CHEM :        4 TERMS
L7          1403 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6
L8            46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L9        284865 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("X-RAY DIFFRACTION"/CV OR
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L11        33989 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALCOHOL/BI
L12         1280 SEA FILE=REGISTRY ABB=ON  PLU=ON  SOLVENT/BI
L13            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHANOL/CN OR ETHANOL/CN OR
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L14          411 SEA FILE=REGISTRY ABB=ON  PLU=ON  GELATIN/BI
L15              SEL  PLU=ON  L13 1- CHEM :       89 TERMS
L16     1231961 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15
L17     1925635 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR L11 OR ALCOHOL OR
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L18      176616 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR GELATIN
L19      963610 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR SOLVENT
L20           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L9
L22           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L18
L23          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L19
L24          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND (L9 OR L17 OR L18 OR
                 L19)
L25          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)L17
L26          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 OR L22 OR L23 OR L24 OR
                 L25
L27     1727804 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
                 INJECTIONS, I.V."+ALL/CV OR ?INTRAVEN? OR ?DRUG? OR ?THERAP?
                 OR ?MEDIC? OR ?PHARMA? OR DRUG DELIVERY?/CV
L29          156 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L7 OR L8)(L)L27) NOT L26
L30            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND ?INTRAVE?
L31           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND PD=<MARCH 4, 2002
L32           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 NOT L30


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=>

=> d ibib abs hitstr l32 1-28

L32  ANSWER 1 OF 28  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:52271  HCAPLUS
DOCUMENT NUMBER:          139:172905
TITLE:                    Histone acetylation and retinoic acid receptor β
                          DNA methylation as novel targets for gastric cancer
                          therapy
AUTHOR(S):                Tahara, Eiichi
CORPORATE SOURCE:         Hiroshima Cancer Seminar Foundation, Radiation Effects
                          Research Foundation, Hiroshima University, Minami-ku,
                          Horoshima, 732-0815, Japan
```
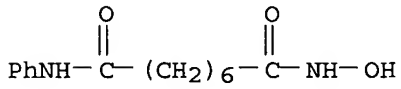

SOURCE: Drug News & Perspectives (2002), 15(9), 581-585
CODEN: DNPEED; ISSN: 0214-0934
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Multiple genetic and epigenetic alterations in oncogenes, tumor-suppressor genes, cell-cycle regulators, cell adhesion mols. and DNA repair genes, as well as genetic instability and telomerase activation, are responsible for tumor genesis and progression of gastric cancer. The scenario of these epigenetic alterations found in gastric cancer differs, depending on the two types of gastric cancer, indicating that there are at least two types of CpG (cytidine phosphate guanosine) island methylator phenotypes in the intestinal-type and diffuse-type of gastric cancer. In addition to promoter methylation, acetylated histone H4 is obviously reduced in a majority of gastric carcinomas. Histone H4 is progressively deacetylated from the early stage (precancerous lesions) to the late stage (invasion and metastasis) in gastric carcinogenesis. Since there is no difference in the level of acetylated histone H4 between the intestinal-type and diffuse-type of gastric cancer, histone H4 deacetylation may be involved in both types of gastric cancer. This review proposes histone acetylation and retinoic acid receptor β DNA methylation as novel targets for gastric cancer therapy.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone acetylation and retinoic acid receptor β (RARβ) DNA methylation as novel targets for gastric cancer therapy)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:651684 HCAPLUS
DOCUMENT NUMBER: 138:198269
TITLE: Suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, suppresses the growth of carcinogen-induced mammary tumors
AUTHOR(S): Cohen, Leonard A.; Marks, Paul A.; Rifkind, Richard A.; Amin, Shantu; Desai, Dhimant; Pittman, Brian; Richon, Victoria M.
CORPORATE SOURCE: American Health Foundation, Valhalla, NY, 10595, USA
SOURCE: Anticancer Research (2002), 22(3), 1497-1504
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, was shown to inhibit the development of N-methylnitrosourea (NMU)-induced rat mammary tumors when fed in the diet continuously for the duration of the carcinogenic process.

The present study was designed to determine whether the inhibitory effects of SAHA occur during the initiation process or at subsequent stages in the carcinogenic process. In addition, animals with established NMU tumors were administered SAHA to determine whether SAHA could inhibit the continued growth of established mammary tumors. It was found that SAHA fed at 900 ppm in the diet inhibited tumor yields when administered from 14 days prior to NMU administration to termination (-14 to +130) and from +14 and +28 days to termination. However, SAHA had no effect on tumor yields when administered from -14 to +14 or from -14 to +50 days and then returned to the control diets for the remainder of the exptl. period (130 days). These results indicate that the inhibitory effects of SAHA are not exerted at the initiation phase of NMU-induced mammary tumorigenesis and appear, instead, to inhibit the subsequent stages in tumor development. Of most interest was the ability of SAHA to inhibit the growth of established mammary tumors. Administration, of SAHA in the diet at 900 ppm resulted in significant inhibition of established tumor growth. Thirty-two percent of SAHA-treated tumors exhibited partial regression compared to 12% of controls, growth was stabilized in 24% of treated tumors compared to 12% of controls while 11% exhibited complete regression compared to 0% of controls. Collectively, SAHA -treated tumors exhibited a 7 fold reduction in growth compared to untreated tumors over the test period. The results of this animal model study indicate that SAHA, when fed in the diet, serves as both a chemopreventive and chemotherapeutic agent in the absence of any detectable side effects.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:618079 HCAPLUS

TITLE: Discovery of NVP-LAQ824: A novel histone deacetylase inhibitor with in vitro and in vivo antitumor activity

AUTHOR(S): Remiszewski, Stacy W.; Sambucetti, Lidia C.; Atadja, Peter; Bair, Kenneth W.; Bontempo, John; Cesarz, David; Chandramouli, Nagarajan; Chen, Ru; Dean, Karl; Diamantidis, George; Green, Michael A.; Howell, Kobporn L.; Kashi, Rina; Kwon, Paul; Lassota, Peter; Mou, Yin; Nemzek, Raphael; Perez, Lawrence B.; Sorensen, Eric; Taplin, Francis, Jr.; Trogani, Nancy; Versace, Richard; Walker, Heather; Weltchek-Engler, Susan; Wood, Alexander W.; Wu, Arthur

CORPORATE SOURCE: Oncology Chemistry, Novartis Pharmaceuticals, Summit, NJ, 07901, USA

SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-227. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Histone acetylation is one major regulator of gene expression which may act by changing the accessibility of transcription factors to DNA or by altering nucleosomal interactions with protein bromodomains. Cell specific patterns of gene expression dependant on histone acetylation result from the competing activities of two classes of enzymes, the histone acetylases and the histone deacetylases (HDACs). Each class is comprised of several isoforms, whose functions are a topic of intense study. Inhibition of HDAC by small mols. has been shown to have antiproliferative effects on tumor cell lines. Recently, there has been

increasing interest in using HDAC inhibitors (HDAIs) as anticancer agents with a novel mechanism of action. Several compds. are in clin. trials, including SAHA, FK-228 and MS-275. We initiated a program to discover novel small mol. HDAIs with the goal being a well-tolerated, efficacious agent equal or superior in vitro and in vivo to those compds. under clin. investigation. A directed medicinal chemical program resulted in the synthesis of several dozen compds. which were profiled in enzyme and cellular assays. Compds. having enzyme IC50s < 200 nM and cellular growth inhibition IC50s < 750 nM were selected for efficacy studies in athymic mice implanted with human tumor xenografts. These efforts led to the discovery of NVP-LAQ824, a representative of a new class of hydroxamic acid HDAI. We present here an overview of the structure-activity relationship for the NVP-LAQ824 class of HDAI and the in vitro and in vivo profile of NVP-LAQ824 which led to its selection for clin. investigation.

L32 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:617973 HCAPLUS
TITLE: Discovery of novel histone deacetylase inhibitors by molecular docking and database screening
AUTHOR(S): Park, Hyun-Ju; Yoo, Jakyung; Kim, Yong Kee; Han, Jeung-Whan; Lee, Hyang-Woo
CORPORATE SOURCE: College of Pharmacy, Sungkyunkwan University, Suwon, 440-746, S. Korea
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-120. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Several histone deacetylase (HDAC) inhibitors, such as trichostatin A, suberoylanilide hydroxamic acid, trapoxin, and apicidin inhibit the growth of several cancer cell lines and induce cell differentiation. HDAC is an emerging target for the treatment of cancer, and the discovery of new HDAC inhibitors as a potential anticancer appears highly desirable. As part of our efforts to find novel small mol. HDAC inhibitors, a computational screening of more than 500,000 organic compds. contained in com. available databases was conducted. Fast docking programs, DOCK and FlexX combined with CScore, were used for mol. docking and scoring of the mols. that are compatible with the catalytic domain of histone deacetylase-like protein. Hydrazone, semicarbazone and carbohydrazone derivs. of trichostatin A straight chain hydroxamate were deliberately chosen, in addition to other families of compds. proposed by docking. About 50 compds. were selected as the high-ranked representatives, and subjected to cell detransforming and HDAC inhibition assay. Some of them were found to inhibit partially purified HDAC in low micromolar range. These compds. are interesting leads for the design of novel HDAC inhibitors and development of potential therapeutic anticancer agents.

L32 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:499899 HCAPLUS
TITLE: Applied Biocatalysis in Specialty Chemicals and Pharmaceuticals by Badal Saha & David Demirjian
AUTHOR(S): Turner, Nick
CORPORATE SOURCE: Dep. Chem., Univ. Edinburgh, UK
SOURCE: Chemistry & Industry (London, United Kingdom) (2002), (12), 30

CODEN: CHINAG; ISSN: 0009-3068
PUBLISHER: Society of Chemical Industry
DOCUMENT TYPE: Journal; Book Review
LANGUAGE: English
AB Unavailable

L32 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:496846 HCAPLUS
DOCUMENT NUMBER: 138:198218
TITLE: Synergistic induction of mitochondrial damage and apoptosis in human leukemia cells by flavopiridol and the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA)
AUTHOR(S): Almenara, J.; Rosato, R.; Grant, S.
CORPORATE SOURCE: Medical College of Virginia, Department of Medicine, Virginia Commonwealth University, Richmond, VA, USA
SOURCE: Leukemia (2002), 16(7), 1331-1343
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interactions between the histone deacetylase inhibitor SAHA (suberoylanilide hydroxamic acid) and the cyclin-dependent kinase (CDK) inhibitor flavopiridol (FP) were examined in human leukemia cells. Simultaneous exposure (24 h) of myelomonocytic leukemia cells (U937) to SAHA (1 μM) and FP (100 nM), which were minimally toxic alone (1.5 and 16.3% apoptosis resp.), produced a dramatic increase in cell death (ie 63.2% apoptotic), reflected by morphol., procaspase-3 and -8 cleavage, Bid activation, diminished ΔΨm, and enhanced cytochrome c release. FP blocked SAHA-mediated up-regulation of p21CIP1 and CD11b expression, while inducing caspase-dependent Bcl-2 and pRb cleavage. Similar interactions were observed in HL-60 and Jurkat leukemic cells. Enhanced apoptosis in SAHA/FP-treated cells was accompanied by a marked reduction in clonogenic survival. Ectopic expression of either dominant-neg. caspase-8 (C8-DN) or CrmA partially attenuated SAHA/FP-mediated apoptosis (eg 45 and 38.2% apoptotic vs 78% in controls) and Bid cleavage. SAHA/FP induced-apoptosis was unaffected by the free radical scavenger L-N-acetyl Cys or the PKC inhibitor GFX. Finally, ectopic Bcl-2 expression marginally attenuated SAHA/FP-related apoptosis/cytochrome c release, and failed to restore clonogenicity in cells exposed to these agents. Together, these findings indicate that SAHA and FP interact synergistically to induce mitochondrial damage and apoptosis in human leukemia cells, and suggest that this process may also involve engagement of the caspase-8-dependent apoptotic cascade.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:479093 HCAPLUS
DOCUMENT NUMBER: 138:18996
TITLE: Histone deacetylase inhibitors and anticancer therapy
AUTHOR(S): Kouraklis, G.; Theocharis, S.
CORPORATE SOURCE: Second Department of Propedeutic Surgery, Medical School University of Athens, Athens, Greece
SOURCE: Current Medicinal Chemistry: Anti-Cancer Agents (2002), 2(4), 477-484
CODEN: CMCACI; ISSN: 1568-0118
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Recent reports have shown that pharmacol. manipulation of chromatin remodeling by histone deacetylase (HDAC) inhibitors, might develop into a potent and specific strategy for the treatment of cancer. Alterations in histone acetylation may lead to changes in chromatin structure and transcriptional dysregulation of genes that are implicated in controlling either cell cycle progression or pathways regulating cell differentiation and/or apoptosis. DMSO was one of the first chems. to be identified as an inducer of transformed cell differentiation. In the class of HDAC inhibitors, now included a short-chain fatty acids, such as 4-phenylbutyrate and valproic acid, hydroxamic acids, such as suberoylanilide hydroxamic acid (SAHA), pyroxamide, trichostatin A, oxamflatin and CHAPSs, cyclic tetrapeptides, such as trapoxin, apicidin and depsipeptide-also known as FK-228 or FR 901228, and benzamides, such as MS-275. First clin. studies have shown that histone hyperacetylation can be achieved safely in humans and that treatment of cancer with such agents seems to become possible. Thus, HDAC inhibitors remains one of the most promising class of new anticancer agents. Further studies are needed to delineate the optimal dosage, the duration of therapy and possibly the efficacy of other agents able to synergize with HDAC inhibitors in the fight against cancer.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:298819 HCAPLUS

DOCUMENT NUMBER: 137:210564

TITLE: Suberoylanilide hydroxamic acid (SAHA) overcomes multidrug resistance and induces cell death in P-glycoprotein-expressing cells

AUTHOR(S): Ruefli, Astrid A.; Bernhard, David; Tainton, Kellie M.; Kofler, Reinhard; Smyth, Mark J.; Johnstone, Ricky W.

CORPORATE SOURCE: Cancer Immunology Division, The Peter MacCallum Cancer Institute, East Melbourne, 3002, Australia

SOURCE: International Journal of Cancer (2002), 99(2), 292-298
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

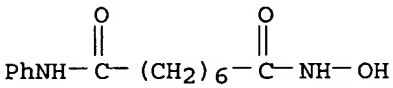
AB Multidrug resistance (MDR) mediated by the ATP-dependent efflux protein P-glycoprotein (P-gp) is a major obstacle to the successful treatment of many cancers. In addition to effluxing toxins, P-gp has been shown to protect tumor cells against caspase-dependent apoptosis mediated by Fas and tumor necrosis factor receptor (TNFR) ligation, serum starvation and UV irradiation However, P-gp does not protect against caspase-independent cell death mediated by granzyme B or pore-forming proteins (perforin, pneumolysin and activated complement). The authors examined the effects of the chemotherapeutic hybrid polar compound suberoylanilide hydroxamic acid (SAHA) on P-gp-expressing MDR human tumor cell lines. In the CEM T-cell line, SAHA, a histone deacetylase inhibitor, induced equivalent death in P-gp-pos. cells compared with P-gp-neg. cells. Cell death was marked by the caspase-independent release of cytochrome c, reactive oxygen species (ROS) production and Bid cleavage that was not affected by P-gp expression. However, consistent with the authors' previous findings, SAHA -induced caspase activation was inhibited in P-gp-expressing cells. These data provide evidence that P-gp inhibits caspase activation after

chemotherapeutic drug treatment and demonstrates that SAHA may be of value for the treatment of P-gp-expressing MDR cancers.

IT 149647-78-9, SAHA
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid overcomes P-glycoprotein-mediated multidrug resistance and induces cell death human tumor cells and mechanism involved)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:190335 HCAPLUS

TITLE: Structurally simple TSA-like straight chain hydroxamates as potent histone deacetylase inhibitors

AUTHOR(S): Woo, Soon Hyung; Bouchain, Giliane; Frechette, Sylvie; Allan, Martin; Abou-Khalil, Elie; Leit, Silvana; Moradei, Oscar; Vaisburg, Arkadii; Bernstein, Naomy; Fournel, Marielle; Yan, Pu T.; Trachy-Bourget, Marie-Claude; Kalita, Ann; Beaulieu, Carole; Li, Zuomei; Macleod, Robert; Besterman, Jeffrey; Delorme, Daniel

CORPORATE SOURCE: Department of Medicinal Chemistry, Methylgene Inc, Montreal, QC, H4S2A1, Can.

SOURCE: Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), MEDI-216. American Chemical Society: Washington, D. C.
CODEN: 69CKQP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Histone deacetylases (HDACs) are critically important in the functional regulation of gene transcription as well as chromatin structure remodeling and have become an emerging target in the search for new anticancer drugs. Several small mol. inhibitors of HDAC, such as the natural product trichostatin A (TSA) and the synthetic compds. suberoylanilide hydroxamic acid (SAHA), and oxamflatin, have been reported to induce differentiation of several cancer cell lines and suppress cell proliferation. As part of our efforts to discover novel HDAC inhibitors, we have synthesized a series of structurally simple TSA-like straight chain hydroxamates by varying chain length, aryl substitution, and aryl-chain connection (e.g. ketone, alkene, oxime etc). Some of these compds. inhibit partially purified human HDAC with IC 50 of low nanomolar range, comparable with those of TSA. These compds. induce hyperacetylation of histones at uM concns. and significantly inhibit proliferation in human cancer cells. They can also induce expression of p21, apoptosis, and cell cycle blocks in human cancer cells. In this presentation we describe synthesis of these new compds. as well as SAR results from enzyme inhibition and cellular potency.

L32 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:190334 HCAPLUS
TITLE: Simple analogs of trichostatin A as potential inhibitors of histone deacetylase
AUTHOR(S): Paul, Brajeswar; Mayer, Bruce F.; Asch, Bonnie; Asch, Harold
CORPORATE SOURCE: Grace Cancer Drug Center, Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
SOURCE: Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), MEDI-215. American Chemical Society: Washington, D. C.
CODEN: 69CKQP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB An antibiotic, trichostatin A (TSA), is a potent inhibitor of histone deacetylase (HDAC) and a highly effective inducer of differentiation in several types of cancer cells. Histones are major determinants of chromatin structure, with acetylation playing a key role in how tightly they bind to DNA and thus regulating accessibility of DNA to transcription factors. Several complex natural products: trapoxin, herbimycin, radicicol, depudecin, apicidin, FR 901228 and a few synthetic congeners: SAHA (suberoylanilide hydroxamic acid) and oxamflatin have been identified as HDAC inhibitors and reported to revert the morphol. changes following the transformation of cells in culture. We have synthesized a set of simple analogs of TSA in as little as five synthetic steps. These compds. are interesting leads for the design of potent inhibitors of HADC and development of potential therapeutic agents for chemoprevention and treatment of cancer. Synthesis, phys. and biol. data will be presented. (Supported by NIH Grant CA16056).

L32 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:914781 HCAPLUS
DOCUMENT NUMBER: 136:193822
TITLE: The histone deacetylase inhibitor suberoylanilide hydroxamic acid induces differentiation of human breast cancer cells
AUTHOR(S): Munster, Pamela N.; Troso-Sandoval, Tiffany; Rosen, Neal; Rifkind, Richard; Marks, Paul A.; Richon, Victoria M.
CORPORATE SOURCE: Program in Cell Biology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Cancer Research (2001), 61(23), 8492-8497
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone deacetylase (HDACs) regulate histone acetylation by catalyzing the removal of acetyl groups on the NH2-terminal lysine residues of the core nucleosomal histones. Modulation of the acetylation status of core histones is involved in the regulation of the transcriptional activity of certain genes. HDAC activity is generally associated with transcriptional repression. Aberrant recruitment of HDAC activity has been associated with the development of certain human cancers. We have developed a class of HDAC inhibitors, such as suberoylanilide hydroxamic acid (SAHA), that were initially identified based on their ability to induce differentiation of cultured murine erythroleukemia cells. Addnl. studies have demonstrated that SAHA inhibits the

growth of tumors in rodents. In this study we have examined the effects of SAHA on MCF-7 human breast cancer cells. We found that SAHA causes the inhibition of proliferation, accumulation of cells in a dose-dependent manner in G1 then G2-M phase of the cell cycle, and induction of milk fat globule protein, milk fat membrane globule protein, and lipid droplets. Growth inhibition was associated with morphol. changes including the flattening and enlargement of the cytoplasm, and a decrease in the nuclear: cytoplasmic ratio. Withdrawal of SAHA led to reentry of cells into the cell cycle and reversal to a less differentiated phenotype. SAHA induced differentiation in the estrogen receptor-neg. cell line SKBr-3 and the retinoblastoma-neg. cell line MDA-468. We propose that SAHA has profound antiproliferative activity by causing these cells to undergo cell cycle arrest and differentiation that is dependent on the presence of SAHA. SAHA and other HDAC inhibitors are currently in Phase I clin. trials. These findings may impact the clin. use of these drugs.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:908905 HCAPLUS

DOCUMENT NUMBER: 137:87961

TITLE: Histone deacetylase inhibitors induce caspase-dependent apoptosis and downregulation of daxx in acute promyelocytic leukaemia with t(15;17)

AUTHOR(S): Amin, Hesham M.; Saeed, Shahnaz; Alkan, Serhan

CORPORATE SOURCE: Department of Pathology, Loyola University Medical Center, Maywood, IL, 60153, USA

SOURCE: British Journal of Haematology (2001), 115(2), 287-297
CODEN: BJHEAL; ISSN: 0007-1048

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histone deacetylase (HDAC) appears to play an important role in the pathogenesis of acute promyelocytic leukemia (APL) as it is recruited by both PML-RARα and PLZF/RARα in leukemic cells with t(15;17) and t(11;17), resp. Recent studies have demonstrated that HDAC inhibitors can be therapeutically used in various neoplastic disorders including APL. Cell differentiation was considered the major mechanism of the anti-leukemic effects of HDAC inhibitors in APL. However, most of these studies either evaluated the effect of HDAC inhibitors in combination with all-trans retinoic acid (ATRA) or focused on the less common form of APL with t(11;17). To investigate the cellular effects of HDAC inhibitors, including sodium butyrate, trichostatin A, and suberoylanilide hydroxamic acid (SAHA), we used two APL cell lines, NB4 and the ATRA-resistant derivative NB4.306. Moreover, primary cells from five patients with cytogenetic evidence for t(15;17) were also studied. Our results demonstrated that HDAC inhibitors induce distinct caspase-dependent apoptosis in APL, which showed both concentration- and time-dependence. In addition, changes in the apoptosis-regulatory proteins, daxx, bcl-2 and bax were analyzed. HDAC inhibitors induced downregulation of daxx, but no significant changes were detected in bcl-2 or bax. In conclusion, apoptosis induced by HDAC inhibitors in APL could provide an effective strategy for treatment of patients with t(15;17).

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

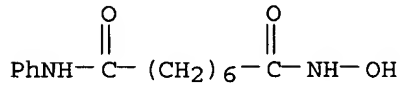
L32 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:867915 HCAPLUS
DOCUMENT NUMBER: 137:72300
TITLE: Histone deacetylase inhibitors as new cancer drugs
AUTHOR(S): Marks, Paul A.; Richon, Victoria M.; Breslow, Ronald; Rifkind, Richard A.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Current Opinion in Oncology (2001), 13(6), 477-483
CODEN: CUOOE8; ISSN: 1040-8746
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Histone deacetylase inhibitors are potent inducers of growth arrest, differentiation, or apoptotic cell death in a variety of transformed cells in culture and in tumor bearing animals. Histone deacetylases and the family of histone acetyl transferases are involved in determining the acetylation of histones, which play a role in regulation of gene expression. Radiograph crystallog. studies reveal that the histone deacetylase inhibitors, suberoylanilide hydroxamic acid and trichostatin A, fit into the catalytic site of histone deacetylase, which has a tubular structure with a zinc atom at its base. The hydroxamic acid moiety of the inhibitor binds to the zinc. Histone deacetylase inhibitors cause acetylated histones to accumulate in both tumor and peripheral circulating mononuclear cells. Accumulation of acetylated histones has been used as a marker of the biol. activity of the agents. Hydroxamic acid-based histone deacetylase inhibitors limit tumor cell growth in animals with little or no toxicity. These compds. act selectively on genes, altering the transcription of only approx. 2% of expressed genes in cultured tumor cells. A number of proteins other than histones are substrates for histone deacetylases. The role that these other targets play in histone deacetylase inducement of cell growth arrest, differentiation, or apoptotic cell death is not known. This review summarizes the characteristics of a variety of inhibitors of histone deacetylases and their effects on transformed cells in culture and tumor growth in animal models. Several structurally different histone deacetylase inhibitors are in phase I or II clin. trials in patients with cancers.

IT 149647-78-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors as new cancer drugs)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:829758 HCAPLUS
DOCUMENT NUMBER: 136:144790
TITLE: Histone deacetylase inhibitors induce remission in transgenic models of therapy-resistant acute promyelocytic leukemia

AUTHOR(S): He, Li-Zhen; Tolentino, Thomas; Grayson, Peter; Zhong, Sue; Warrell, Raymond P., Jr.; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.; Pandolfi, Pier Paolo

CORPORATE SOURCE: Molecular Biology Program and Department of Pathology, Memorial Sloan-Kettering Cancer Center, Sloan-Kettering Division, Graduate School of Medical Sciences, Cornell University, New York, NY, USA

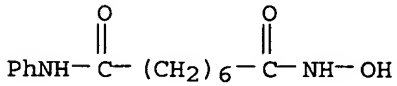
SOURCE: Journal of Clinical Investigation (2001), 108(9), 1321-1330
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acute promyelocytic leukemia (APL) is associated with chromosomal translocations, invariably involving the retinoic acid receptor α (RARα) gene fused to one of several distinct loci, including the PML or PLZF genes, involved in t(15;17) or t(11;17), resp. Patients with t(15;17) APL respond well to retinoic acid (RA) and other treatments, whereas those with t(11;17) APL do not. The PML-RARα and PLZF-RARα fusion oncoproteins function as aberrant transcriptional repressors, in part by recruiting nuclear receptor-transcriptional corepressors and histone deacetylases (HDACs). Transgenic mice harboring the RARα fusion genes develop forms of leukemia that faithfully recapitulate both the clin. features and the response to RA observed in humans with the corresponding translocations. Here, we investigated the effects of HDAC inhibitors (HDACIs) in vitro and in these animal models. In cells from PLZF-RARα/RARα-PLZF transgenic mice and cells harboring t(15;17), HDACIs induced apoptosis and dramatic growth inhibition, effects that could be potentiated by RA. HDACIs also increased RA-induced differentiation. HDACIs, but not RA, induced accumulation of acetylated histones. Using microarray anal., we identified genes induced by RA, HDACIs, or both together. In combination with RA, all HDACIs tested overcame the transcriptional repression exerted by the RARα fusion oncoproteins. In vivo, HDACIs induced accumulation of acetylated histones in target organs. Strikingly, this combination of agents induced leukemia remission and prolonged survival, without apparent toxic side effects.

IT 149647-78-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors induce remission in transgenic models of therapy-resistant acute promyelocytic leukemia)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:829742 HCAPLUS

DOCUMENT NUMBER: 136:112101

TITLE: Targeting aberrant transcriptional repression in leukemia: a therapeutic reality?

AUTHOR(S): Licht, Jonathan D.
CORPORATE SOURCE: Derald H. Ruttenberg Cancer Center and Department of Medicine, Mount Sinai School of Medicine, New York, NY, 10029, USA
SOURCE: Journal of Clinical Investigation (2001), 108(9), 1277-1278
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review on transcription-targeted therapy. The discovery that transcription factors are frequently disrupted in leukemia has led to efforts to target these proteins with drugs. While transcription factors are generally thought not to be "druggable ", the ability of the pathogenic fusion proteins of leukemia to recruit histone deacetylases (HDACs) can indeed be targeted by small organic mols. Suberoylanilide hydroxyamic acid (SAHA) is an HDAC inhibitor that may reverse aberrant repression by fusion proteins. He et al. (2001) showed that only the combination of retinoic acid and SAHA is sufficient to clear leukemic blasts from the peripheral blood of mice harboring the fusion genes of t(11;17) acute promyelocytic leukemia.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:712315 HCAPLUS
DOCUMENT NUMBER: 136:47848
TITLE: Cell cycle regulation in the G1 phase: a promising target for the development of new chemotherapeutic anticancer agents
AUTHOR(S): Owa, Takashi; Yoshino, Hiroshi; Yoshimatsu, Kentaro; Nagasu, Takeshi
CORPORATE SOURCE: Laboratory of Seeds Finding Technology, Eisai Co., Ltd., Tsukuba, 300-2635, Japan
SOURCE: Current Medicinal Chemistry (2001), 8(12), 1487-1503
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. As a result of substantial advances in recent cancer biol., cell cycle regulation in the G1 phase has attracted a great deal of attention as a promising target for the research and treatment of cancer. Many of the important genes associated with G1 regulation have been shown to play a key role in proliferation, differentiation and oncogenic transformation and programmed cell death (apoptosis). Currently, a variety of "cytostatic" agents that affects G1 progression and/or G1/S transition are being evaluated in clin. trials. Flavopiridol is a potent inhibitor of cyclin-dependent kinases (CDKs). UCN-01 was originally a PKC-selective protein kinase antagonist. More recent studies have revealed that this agent can also inhibit several CDKs and the checkpoint kinase CHK1. FR901228, MS-27-275 and SAHA are histone deacetylase inhibitors that induce changes in the transcription of specific genes via the hyperacetylation of histones. The proteasome inhibitor PS-341 disrupts the degradation process of intracellular proteins, including cell cycle regulatory proteins such as cyclins. RI15777, SCH66336 and BMS-214662 are non-peptidic farnesyl transferase inhibitors that prevent p21 ras oncogene activation. Rapamycin derivative CCI-779 downregulates signals through S6 kinase and FRAP (FKBP-rapamycin associating protein), affecting the expression levels of mRNAs important for

progression from G1 to S phase. 17-Allylaminogeldanamycin targets the Hsp-90 (heat shock protein-90) family of cellular chaperones regulating the function of signaling proteins. TNP-470 (AGM-1470), a fumagillin derivative shows antiangiogenic action through binding to MetAP-2 (methionine aminopeptidase-2). The antitumor sulfonamide E7070, causing a cellular accumulation in the G1 phase, has been shown to suppress the activation of CDK2 and cyclin E expression in HCT116 colorectal cancer cell line highly sensitive to the drug. With respect to several growth factor receptors such as EGFR, PDGFR, bFGFR and VEGFR, potent and specific inhibitors of receptor tyrosine kinases have been also examined as hopeful drug candidates. In this report, we review the current status of extensive efforts directed towards the discovery and development of new chemotherapeutic anticancer agents targeting cell cycle regulation in the G1 phase, with particular focus on the compds. undergoing clin. investigations.

REFERENCE COUNT: 193 THERE ARE 193 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

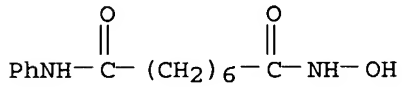
L32 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:705528 HCAPLUS
DOCUMENT NUMBER: 136:63692
TITLE: The histone deacetylase inhibitor and chemotherapeutic agent suberoylanilide hydroxamic acid (SAHA) induces a cell-death pathway characterized by cleavage of Bid and production of reactive oxygen species
AUTHOR(S): Ruefli, Astrid A.; Ausserlechner, Michael J.; Bernhard, David; Sutton, Vivien R.; Tainton, Kellie M.; Kofler, Reinhard; Smyth, Mark J.; Johnstone, Ricky W.
CORPORATE SOURCE: Cancer Immunology Division, The Peter MacCallum Cancer Institute, Trescowthick Research Laboratories, East Melbourne, 3002, Australia
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(19), 10833-10838
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many chemotherapeutic agents induce mitochondrial-membrane disruption to initiate apoptosis. However, the upstream events leading to drug-induced mitochondrial perturbation have remained poorly defined. We have used a variety of physiol. and pharmacol. inhibitors of distinct apoptotic pathways to analyze the manner by which suberoylanilide hydroxamic acid (SAHA), a chemotherapeutic agent and histone deacetylase inhibitor, induces cell death. We demonstrate that SAHA initiates cell death by inducing mitochondria-mediated death pathways characterized by cytochrome c release and the production of reactive oxygen species, and does not require the activation of key caspases such as caspase-8 or -3. We provide evidence that mitochondrial disruption is achieved by means of the cleavage of the BH3-only proapoptotic Bcl-2 family member Bid. SAHA-induced Bid cleavage was not blocked by caspase inhibitors or the overexpression of Bcl-2 but did require the transcriptional regulatory activity of SAHA. These data provide evidence of a mechanism of cell death mediated by transcriptional events that result in the cleavage of Bid, disruption of the mitochondrial membrane, and production of reactive oxygen species to induce cell death.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:381216 HCAPLUS
DOCUMENT NUMBER: 135:131735
TITLE: 3-(4-Aroyl-1H-pyrrol-2-yl)-N-hydroxy-2-propenamides, a new class of synthetic histone deacetylase inhibitors
AUTHOR(S): Massa, Silvio; Mai, Antonello; Sbardella, Gianluca; Esposito, Monica; Ragno, Rino; Loidl, Peter; Brosch, Gerald
CORPORATE SOURCE: Dipartimento Farmaco Chimico Tecnologico, Universita degli Studi di Siena, Siena, 53100, Italy
SOURCE: Journal of Medicinal Chemistry (2001), 44(13), 2069-2072
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:131735

AB Novel 3-(4-aroyl-2-pyrrolyl)-N-hydroxy-2-propenamides are disclosed as a new class of histone deacetylase (HDAC) inhibitors. Three-dimensional structure-based drug design and conformational analyses into the histone deacetylase-like protein (HDLP) catalytic core suggested the synthesis and biol. evaluation of compds. 7a-h. Exptl. pKi values are in good agreement with VALIDATE predicted pKi values of new derivs. All compds. 7a-h show HDAC inhibitory activity in the micromolar range, with 7e as the most potent derivative (IC50 = 1.9 μM). The influence of the 4'-substituent in the aroyl moiety is not significant for the inhibitory activity, as all compds. 7a-g show IC50 values between 1.9 and 3.9 μM. Otherwise, the unsatd. chain linking the pyrrole ring to the hydroxamic acid group is clearly important for the anti-HDAC activity, the saturated analog 7h being 10-fold less active than the unsatd. counterpart 7a.

IT 149647-78-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(structure-based drug design of synthetic histone deacetylase inhibitors)
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:159813 HCAPLUS
DOCUMENT NUMBER: 134:320438
TITLE: New agents in cancer clinical trials
AUTHOR(S): Adams, Julian; Elliott, Peter J.
CORPORATE SOURCE: Millennium Pharmaceuticals, Inc., Cambridge, MA, 02139, USA
SOURCE: Oncogene (2000), 19(56), 6687-6692
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 75 refs. With advances in modern technologies and growing understanding of cellular biol., a variety of new mechanism and mol. antagonists are highlighted as possible new therapies which may add to the much needed armamentarium of cancer drugs. Some of these new mol. antagonists are proteasome inhibitor, PS-341; HSP 90 inhibitor, geldanamycin; histone deacetylase inhibitor, SAHA; anti-angiogenic tubulin binding agent, Combretastatin A4 phosphate; a minor-grove DNA inhibitor, ET-743; antifolates; and a protein tyrosine kinase inhibitor, STI-571.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:821360 HCAPLUS

DOCUMENT NUMBER: 134:361062

TITLE: Suberoylanilide hydroxamic acid as a potential therapeutic agent for human breast cancer treatment

AUTHOR(S): Huang, Lili; Pardee, Arthur B.

CORPORATE SOURCE: Division of Cancer Biology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Molecular Medicine (New York) (2000), 6(10), 849-866
CODEN: MOMEF3; ISSN: 1076-1551

PUBLISHER: Johns Hopkins University Press

DOCUMENT TYPE: Journal

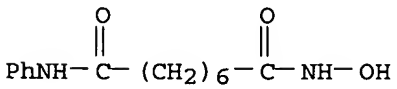
LANGUAGE: English

AB Suberoylanilide hydroxamic acid (SAHA) is a prototype of the newly developed, 2nd-generation, hybrid polar compds. It is a novel histone deacetylase inhibitor with high potency for inducing cell differentiation of cultured murine erythroleukemia cells. Human breast cancer cell lines MCF7, MDA-MB-231, and MDA-MB-435, as well as normal cells, including the normal breast epithelial cell line MCF-10A, and fibroblasts, were treated with SAHA. SAHA induced growth inhibition, cell cycle arrest, and eventual apoptosis in the breast cancer cells, possibly by modulating cell cycle- and apoptosis-regulatory proteins, such as cyclin-dependent kinase inhibitors p21 and p27, pRb, and other differentiation- and/or growth inhibition-associated genes, including gelsolin, isopentenyl diphosphate δ-isomerase and 1,25-dihydroxyvitamin D3 up-regulated protein 1. This, together with the low toxicity in normal cells, suggests that SAHA might have therapeutic potential for the treatment of human breast cancers.

IT 149647-78-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid as potential therapeutic agent for human breast cancer treatment)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:633220 HCAPLUS
DOCUMENT NUMBER: 133:360372
TITLE: Histone deacetylase inhibitor selectively induces p21WAF1 expression and gene-associated histone acetylation
AUTHOR(S): Richon, Victoria M.; Sandhoff, Todd W.; Rifkind, Richard A.; Marks, Paul A.
CORPORATE SOURCE: DeWitt Wallace Research Laboratory, Cell Biology Program, Memorial Sloan-Kettering Cancer Center and Graduate School of Medical Sciences of Cornell Medical School, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(18), 10014-10019
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone deacetylases (HDACs) catalyze the removal of acetyl groups on the amino-terminal lysine residues of core nucleosomal histones. This activity is associated generally with transcriptional repression. We have reported previously that inhibition of HDAC activity by hydroxamic acid-based hybrid polar compds., such as suberoylanilide hydroxamic acid (SAHA), induces differentiation and/or apoptosis of transformed cells in vitro and inhibits tumor growth in vivo. SAHA is a potentially new therapeutic approach to cancer treatment and is in Phase I clin. trials. In several tumor cell lines examined, HDAC inhibitors alter the expression of less than 1% of expressed genes, including the cell cycle kinase inhibitor p21WAF1. In T24 bladder carcinoma cells, SAHA induces up to a 9-fold increase in p21WAF1 mRNA and protein, which is, at least in part, because of an increase in the rate of transcription of the gene. SAHA causes an accumulation of acetylated histones H3 and H4 in total cellular chromatin by 2 h, which is maintained through 24 h of culture. An increase in the accumulation of acetylated H3 and H4 was detected throughout the p21WAF1 promoter and the structural gene after culture with SAHA. The level of histone acetylation did not change in chromatin associated with the actin and p27 genes, and their mRNA expression was not altered during culture of T24 cells with SAHA . Thus, the present findings indicate that the induction of p21WAF1 by SAHA is regulated, at least in part, by the degree of acetylation of the gene-associated histones and that this induced increase in acetylation is gene selective.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:598231 HCAPLUS
DOCUMENT NUMBER: 134:50882
TITLE: Histone deacetylase inhibitors: inducers of differentiation or apoptosis of transformed cells
AUTHOR(S): Marks, Paul A.; Richon, Victoria M.; Rifkind, Richard A.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SOURCE: Journal of the National Cancer Institute (2000), 92(15), 1210-1216
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 84 refs. Histone deacetylase (HDAC) inhibitors have been shown to be potent inducers of growth arrest, differentiation, and/or apoptotic cell death of transformed cells in vitro and in vivo. One class of HDAC inhibitors, hydroxamic acid-based hybrid polar compds. (HPCs), induce differentiation at micromolar or lower concns. Studies (x-ray crystallog.) showed that the catalytic site of HDAC has a tubular structure with a zinc atom at its base and that these HDAC inhibitors, such as suberoylanilide hydroxamic acid and trichostatin A, fit into this structure with the hydroxamic moiety of the inhibitor binding to the zinc. HDAC inhibitors cause acetylated histones to accumulate in both tumor and normal tissues, and this accumulation can be used as a marker of the biol. activity of the HDAC inhibitors. Hydroxamic acid-based HPCs act selectively to inhibit tumor cell growth at levels that have little or no toxicity for normal cells. These compds. also act selectively on gene expression, altering the expression of only about 2% of the genes expressed in cultured tumor cells. In general, chromatin fractions enriched in actively transcribed genes are also enriched in highly acetylated core histones, whereas silent genes are associated with nucleosomes with a low level of acetylation. However, HDACs can also acetylate proteins other than histones in nucleosomes. The role that these other targets play in the induction of cell growth arrest, differentiation, and/or apoptotic cell death has not been determined Our working hypothesis is that inhibition of HDAC activity leads to the modulation of expression of a specific set of genes that, in turn, result in growth arrest, differentiation, and/or apoptotic cell death. The hydroxamic acid-based HPCs are potentially effective agents for cancer therapy and, possibly, cancer chemoprevention.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:722502 HCAPLUS
DOCUMENT NUMBER: 132:298585
TITLE: Permeability characteristics of air-interface primary rabbit conjunctival epithelial cell culture
AUTHOR(S): Yang, J. J.; Lee, V. H. L.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Southern California, Los Angeles, CA, 90033, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 835-836
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In 1996, Saha et. al. reported the development of a functional primary culture of rabbit conjunctival epithelial cells in liquid covered condition for evaluating drug permeability characteristics. However, these cultured cell layers exhibited 44% higher transepithelial elec. resistance (TEER) compared with the excised tissue. Our results showed that the TEER of air interface culture of rabbit conjunctival epithelial cells mimics the tissue better than liquid-covered culture. The permeability of the cell layers was comparable with the tissue for polar solutes but is lower for lipophilic compds.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:351946 HCAPLUS
DOCUMENT NUMBER: 131:111064
TITLE: Photoaffinity labeling and mass spectrometry identify ribosomal protein S3 as a potential target for hybrid polar cytodifferentiation agents
AUTHOR(S): Webb, Yael; Zhou, Xianbo; Ngo, Lang; Cornish, Virginia; Stahl, Oachim; Erdjument-Bromage, Hediye; Tempst, Paul; Rifkind, Richard A.; Marks, Paul A.; Breslow, Ronald; Richon, Victoria M.
CORPORATE SOURCE: Department of Chemistry, Columbia University, New York, NY, 10027, USA
SOURCE: Journal of Biological Chemistry (1999), 274(20), 14280-14287
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of a novel class of hybrid polar compds. (HPCs) to induce differentiation and consequent cessation of proliferation of transformed cells has led to their development as potential chemotherapeutic agents in the treatment of cancer. Suberoylanilide hydroxamic acid (SAHA) is a prototype of a family of hydroxamic acid based compds. (SAHA-like HPCs) that can, at micromolar concns., induce a variety of transformed cell lines to differentiate. The mechanism of action of the HPCs is not entirely understood. Searching for a cellular target of the SAHA-like HPCs, we synthesized a photoaffinity labeling reagent structurally based on SAHA, and probed for SAHA-binding proteins in murine erythroleukemia (MEL) cells. Photoaffinity labeling in cell free exts. identified a 32-kDa protein (p32) that was specifically labeled by the photoaffinity reagent. Cell fractionation assays localized p32 to the P100 fraction. p32 was partially purified and identified by mass spectrometry as the 40 S ribosomal protein S3. Expression of epitope-tagged S3 in bacterial lysates followed by photoaffinity labeling confirmed its specific labeling. Identification of a cytodifferentiation agent target may shed light on the mechanism by which the SAHA -like HPCs exert their antitumor effects.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:124870 HCAPLUS
TITLE: Fundamentals of nuclear pharmacy, 4th Ed, By Gopal b. Saha
AUTHOR(S): Sayed, Gary M.
CORPORATE SOURCE: Bowling Green, OH, 43402, USA
SOURCE: Health Physics (1999), 76(2), 197-198
CODEN: HLTPAO; ISSN: 0017-9078
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; Book Review
LANGUAGE: English
AB Unavailable

L32 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:366979 HCAPLUS

DOCUMENT NUMBER: 125:104239
TITLE: Second generation hybrid polar compounds are potent inducers of transformed cell differentiation
AUTHOR(S): Richon, V. M.; Webb, Y.; Merger, R.; Sheppard, T.; Jursic, B.; Ngo, L.; Civoli, F.; Breslow, R.; Rifkind, R. A.; Marks, P. A.
CORPORATE SOURCE: Program of Cell Biology and Genetics, DeWitt Wallace Res. Laboratories, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(12), 5705-5708
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hybrid polar compds., of which hexamethylenebisacetamide (HMBA) is the prototype, are potent inducers of differentiation of murine erythroleukemia (MEL) cells and a wide variety of other transformed cells. HMBA has been shown to induce differentiation of neoplastic cells of dose-limiting toxicity. The authors report on a group of three potent second generation hybrid polar compds., di-Et bis-(pentamethylene-N,N-dimethylcarboxamide)malonate (EMBA), suberoylanilide hydroxamic acid (SAHA), and m-carboxycinnamic acid bis-hydroxamide (CBHA) with optimal concns. for inducing MEL cells of 0.4 mM, 2 μM, and 4 μM, resp., compared to 5 mM for HMBA. All three agents induce accumulation of underphosphorylated pRB; increased levels of p21 protein, a prolongation of the initial G1 phase of the cell cycle; and accumulation of Hb. However, based upon their effective concns., the cross-resistance or sensitivity of an HMBA-resistant MEL cell variant, and differences in c-myb expression during induction, these differentiation-inducing hybrid polar compds. can be grouped into two subsets, HMBA/EMBA and SAHA/CBHA. This classification may prove of value in selecting and planning prospective preclin. and clin. studies toward the treatment of cancer by differentiation therapy.

L32 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:548545 HCAPLUS
DOCUMENT NUMBER: 109:148545
TITLE: Meghnad Saha Medal Lecture - 1987. Ayurveda and modern drug development
AUTHOR(S): Dev, Sukh
CORPORATE SOURCE: Malti-Chem Res. Cent., Vadodara, India
SOURCE: Proceedings of the Indian National Science Academy, Part A: Physical Sciences (1988), 54(1), 12-42
CODEN: PIPSBD; ISSN: 0370-0046
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A lecture by the recipient of the 1987 Meghnad Saha Medal dealing with ayurveda in the development of modern drugs.

L32 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:506136 HCAPLUS
DOCUMENT NUMBER: 99:106136
TITLE: Laser microprobe mass analysis of doped epoxy resin standards
AUTHOR(S): Wieser, P.; Wurster, R.; Seiler, H.
CORPORATE SOURCE: Inst. Phys., Univ. Hohenheim, Stuttgart, D-7000/70, Fed. Rep. Ger.
SOURCE: Scanning Electron Microscopy (1982), (4),

1435-41
CODEN: SEMYBL; ISSN: 0586-5581
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thin sections of epoxy resin stds. doped with crown ether complexes of the elements Li, Na, K, Sr and Pb were used to determine relative sensitivity factors by means of a laser microprobe mass analyzer (LAMMA). Simple models for the laser induced ionization process, based on the well known Saha-Eggert equation cannot explain the exptl. values. A discrepancy of more than one order of magnitude is observed for Pb, even if mass discrimination of the detection system (ion electron conversion) is taken into account. For a better understanding of the measurements the laser induced evaporation must be considered too. The qual. interpretation of time-of-flight mass spectra obtained from pure crown ether complexes, besides the cation, yields the mass lines of cationized crown ether mols., also observed in the corresponding field desorption mass spectra. If embedded in epoxy resin, these cationized crown ether mol. mass lines do not appear in the spectra, revealing a severe matrix effect, probably existing for the cation also and thus limiting the practicability of these stds. for quantitation in biomedical LAMMA applications.

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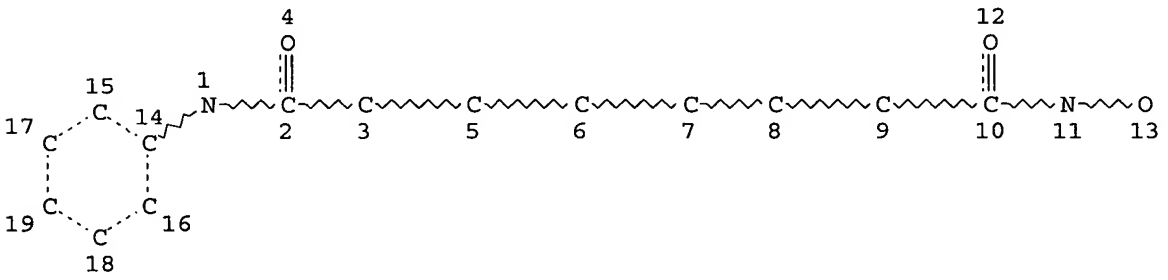

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
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L5 180 SEA FILE=REGISTRY ABB=ON PLU=ON L4 NOT L1
L6 SEL PLU=ON L1 1- CHEM : 4 TERMS
L7 1403 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
L8 46 SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L9 284865 SEA FILE=HCAPLUS ABB=ON PLU=ON ("X-RAY DIFFRACTION"/CV OR "KOSSEL EFFECT"/CV OR XRD/CV) OR X(W)RAY(W)DIFFRACTION
L10 76645 SEA FILE=HCAPLUS ABB=ON PLU=ON "DIFFERENTIAL SCANNING CALORIMETRY"/CV OR DIFFERENTIAL(W) SCANNING(W) CALORIMETRY OR DSC
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L19       963610 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR SOLVENT
L20            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L9
L22            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L18
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L24           12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND (L9 OR L17 OR L18 OR
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L33          644 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("MILLER THOMAS"/AU OR
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                 L9 OR L10 OR L17 OR L18)
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L38           88 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L35 OR L37) NOT (L26 OR L30
                 OR L31)


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L38  ANSWER 1 OF 88  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:177856  HCAPLUS
DOCUMENT NUMBER:          142:254579
TITLE:                    Method of treating cancer with histone deacetylase
                          (HDAC) inhibitors
INVENTOR(S):              Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller,
                          Thomas A.; Paradise, Carolyn M.; Richon,
                          Victoria M.
PATENT ASSIGNEE(S):       Aton Pharma, Inc., USA; Sloan-Kettering Institute for
                          Cancer Research
SOURCE:                   PCT Int. Appl., 107 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   7
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018578	A2	20050303	WO 2004-US27943	20040826
WO 2005018578	A3	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004087631	A1	20040506	US 2003-650025	20030826
US 2004127523	A1	20040701	US 2003-665079	20030916
AU 2004266169	A1	20050303	AU 2004-266169	20040826
AU 2004266169	A2	20050303		
CA 2535806	AA	20050303	CA 2004-2535806	20040826
EP 1663194	A2	20060607	EP 2004-782425	20040826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:	US 2003-650025	A1 20030826
	US 2003-655079	A 20030916
	US 2003-665079	A1 20030916
	US 2002-361759P	P 20020304
	US 2003-379149	A2 20030304
	WO 2004-US27943	W 20040826

OTHER SOURCE(S): MARPAT 142:254579

AB The invention discloses methods for treating cancers, e.g. mesothelioma or lymphoma. More specifically, the invention discloses methods for treating mesothelioma or diffuse large B-cell lymphoma (DLBCL), by administration of pharmaceutical compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid (SAHA; preparation described). The oral formulations of the pharmaceutical compns. have favorable pharmacokinetic profiles such as high bioavailability and surprisingly give rise to high blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo.

L38 ANSWER 2 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:1034586 HCAPLUS
DOCUMENT NUMBER:	142:290399
TITLE:	Histone deacetylase inhibitors
AUTHOR(S):	Marks, Paul A.; Richon, Victoria M.; Miller, Thomas; Kelly, William Kevin
CORPORATE SOURCE:	Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE:	Advances in Cancer Research (2004), 91, 137-168 CODEN: ACRSAJ; ISSN: 0065-230X
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. The base sequence of DNA provides the genetic code for proteins. The regulation of expression or suppression of gene transcription is largely determined by the structure of the chromatin-referred to as epigenetic gene regulation (Agalioti et al., 2002; Jenuwein and Allis, 2001; Richards and Elgin, 2002; Spotswood and Turner, 2002; Zhang

and Reinberg, 2001). Posttranslational modifications of the histones of chromatin play an important role in regulating gene expression. Some of the most extensively studied epigenetic modifications involve acetylation/deacetylation of lysines in the tails of the core histones, which is controlled by the action of histone deacetylases (HDACs) and histone acetyltransferases (HATs). A controlled balance between histone acetylation and deacetylation appears to be essential for normal cell growth (Waterborg, 2002). Alterations in the structure or expression of HATs and HDACs occur in many cancers (Jones and Baylin, 2002; Marks et al., 2001, 2003; Timmermann et al., 2001; Wang et al., 2001). A structurally diverse group of mols. has been developed that can inhibit HDACs (HDACi) (Arts et al., 2003; Bouchain and Delorme, 2003; Curtin and Glase 2003; Johnstone and Licht, 2003; Marks et al., 2003; Remiszewski, 2003; Richon et al., 1998; Yoshida et al., 2003). These inhibitors induce growth arrest, differentiation, and/or apoptosis of cancer cells in vitro and in in vivo tumor-bearing animal models. Clin. trials with several of these agents have shown that certain HDACi have antitumor activity against various cancers at doses that are well tolerated by patients.

REFERENCE COUNT: 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:878268 HCAPLUS
DOCUMENT NUMBER: 141:360666
TITLE: Hydroxamic acid compounds for the inhibition of histone deacetylase, preparation thereof, and use in the treatment of cancer and other conditions
INVENTOR(S): Breslow, Ronald; Miller, Thomas A.; Belvedere, Sandro; Marks, Paul A.; Richon, Victoria M.; Rifkind, Richard A.
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA; The Trustees of Columbia University In the City of New York
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089293	A2	20041021	WO 2004-US10250	20040401
WO 2004089293	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2004228011	A1	20041021	AU 2004-228011	20040401
CA 2520611	AA	20041021	CA 2004-2520611	20040401
US 2004266818	A1	20041230	US 2004-817688	20040401
EP 1613592	A2	20060111	EP 2004-749691	20040401

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-459826P P 20030401
WO 2004-US10250 W 20040401

OTHER SOURCE(S): MARPAT 141:360666

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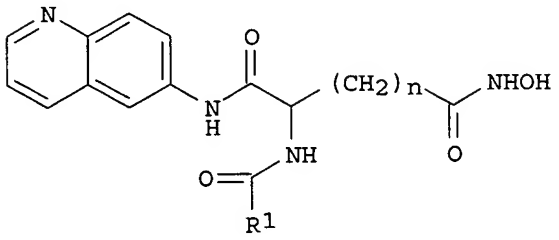

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AB The invention discloses hydroxamic acid derivs. having at least two aryl-containing groups, at least one of which is a quinolinyl, isoquinolinyl or benzyl moiety, linked to the hydroxamic acid group through a methylene chain. The hydroxamic acid compds. can be used to treat cancer, e.g. brain cancer. The hydroxamic acid compds. can also inhibit histone deacetylase and are suitable for use in selectively inducing terminal differentiation, and arresting cell growth and/or apoptosis of neoplastic cells, thereby inhibiting proliferation of such cells. Thus, the compds. of the invention are useful in treating a patient having a tumor characterized by proliferation of neoplastic cells. Preparation of compds., e.g. I, is described.

L38 ANSWER 4 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:761215 HCAPLUS
DOCUMENT NUMBER: 142:126263
TITLE: Histone deacetylase inhibitors: development as cancer therapy
AUTHOR(S): Marks, Paul A.; Richon, Victoria M.; Kelly, Wm. Kevin; Chiao, Judy H.; Miller, Thomas
CORPORATE SOURCE: Cell Biology Program, Sloan Kettering Institute, Memorial Sloan-Kettering Cancer Center, NY, USA
SOURCE: Novartis Foundation Symposium (2004), 259(Reversible Protein Acetylation), 269-284
CODEN: NFSYF7; ISSN: 1528-2511
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Historic deacetylase (HDAC) inhibitors represent a new class of targeted anticancer agents. A number of structural classes of HDAC inhibitors have been developed of which several are in clin. trials, including phenylbutyrate (PB) and related compds.; the hydroxamic acids, suberoylanilide hydroxamic acid (SAHA) and depsipeptide (FK-228); and the benzamides, MS-275 and C1-994. This review will focus on our studies with the hydroxamic acid HDAC inhibitors, of which SAHA is the lead agent. X-ray crystallog. studies with a HDAC homolog (HDLP) demonstrated that the hydroxamic acid group, most of the aliphatic chain and part of the Ph amino group of SARA inserts into the pocket-like catalytic site of the enzyme, at the base of which is a zinc mol. SAHA inhibits the activity of class I and II HDACs and is selective in altering gene expression. SAHA is synergistic in its anticancer activity with radiation, kinase inhibitors,

cytotoxic agents and differentiating agents. In phase I clin. trial with orally administered SAHA the agent caused accumulation of acetylated histones in peripheral mononuclear cells and tumor cells, has excellent bioavailability and has shown antitumor activity in patients with haematol. and solid tumors.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:550755 HCAPLUS
DOCUMENT NUMBER: 141:82311
TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2004 72,735.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004132825	A1	20040708	US 2003-692523	20031024
US 2004072735	A1	20040415	US 2003-379149	20030304
AU 2004283717	A2	20050506	AU 2004-283717	20041022
AU 2004283717	A1	20050506		
CA 2543319	AA	20050506	CA 2004-2543319	20041022
WO 2005039498	A2	20050506	WO 2004-US35181	20041022
WO 2005039498	A3	20051124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1689379	A2	20060816	EP 2004-796215	20041022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:

US 2002-361759P	P	20020304
US 2003-379149	A2	20030304
US 2003-692523	A	20031024
WO 2004-US35181	W	20041022

OTHER SOURCE(S): MARPAT 141:82311

AB The invention discloses methods for treating cancers, e.g. leukemia. More specifically, the invention relates to methods of treating acute and chronic leukemias including Acute Lymphocytic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphocytic leukemia (CLL), Chronic myeloid leukemia (CML) and Hairy Cell Leukemia, by administration of pharmaceutical compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid (SAHA; preparation described). The oral formulations of the

pharmaceutical compns. have favorable pharmacokinetic profiles such as high bioavailability and surprisingly give rise to high blood levels of the active compds. over an extended period. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo.

L38 ANSWER 6 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:533980 HCAPLUS
DOCUMENT NUMBER: 141:65091
TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Cont.-in-part of U.S. Ser. No. 379,149.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127523	A1	20040701	US 2003-665079	20030916
US 2004072735	A1	20040415	US 2003-379149	20030304
AU 2004266169	A1	20050303	AU 2004-266169	20040826
AU 2004266169	A2	20050303		
CA 2535806	AA	20050303	CA 2004-2535806	20040826
WO 2005018578	A2	20050303	WO 2004-US27943	20040826
WO 2005018578	A3	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1663194	A2	20060607	EP 2004-782425	20040826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:

US 2002-361759P	P	20020304
US 2003-379149	A2	20030304
US 2003-650025	A	20030826
US 2003-655079	A	20030916
US 2003-665079	A	20030916
WO 2004-US27943	W	20040826

OTHER SOURCE(S): MARPAT 141:65091

AB The invention relates to methods of treating cancers, e.g., lymphoma. More specifically, the present invention relates to methods of treating diffuse large B-cell lymphoma (DLBCL), by administration of pharmaceutical compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid (preparation described). The oral formulations of the pharmaceutical compns. have favorable pharmacokinetic profiles such as high bioavailability and

surprisingly give rise to high blood levels of the active compds. over an extended period of time. The present invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo.

L38 ANSWER 7 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:533979 HCAPLUS
DOCUMENT NUMBER: 141:65090
TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors
INVENTOR(S): Chiao, Judy H.; Bacopoulos, Nicholas G.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 56 pp., Cont.-in-part of U.S. Ser. No. 379,149.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004127522	A1	20040701	US 2003-616649		20030709
US 2004072735	A1	20040415	US 2003-379149		20030304
PRIORITY APPLN. INFO.:			US 2002-361759P	P	20020304
			US 2003-379149	A2	20030304

OTHER SOURCE(S): MARPAT 141:65090
AB The invention provides methods for treating cancers, chemoprevention, selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. Compds. of the invention include e.g. suberoylanilide hydroxamic acid (preparation described).

L38 ANSWER 8 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:372881 HCAPLUS
DOCUMENT NUMBER: 140:368663
TITLE: Methods of treating cancer with hydroxamic acid derivative histone deacetylase (HDAC) inhibitors
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 379,149.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004087631	A1	20040506	US 2003-650025	20030826
US 2004072735	A1	20040415	US 2003-379149	20030304
AU 2004266169	A1	20050303	AU 2004-266169	20040826
AU 2004266169	A2	20050303		
CA 2535806	AA	20050303	CA 2004-2535806	20040826
WO 2005018578	A2	20050303	WO 2004-US27943	20040826
WO 2005018578	A3	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1663194	A2	20060607	EP 2004-782425	20040826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006167103	A1	20060727	US 2006-391971	20060328
PRIORITY APPLN. INFO.:			US 2002-361759P	P 20020304
			US 2003-379149	A2 20030304
			US 2003-650025	A 20030826
			US 2003-655079	A 20030916
			US 2003-665079	A 20030916
			WO 2004-US27943	W 20040826

OTHER SOURCE(S): MARPAT 140:368663

AB The invention provides methods for treating cancers (e.g. mesothelioma), chemoprevention, selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. HDAC inhibitors of the invention are hydroxamic acid derivs. e.g. suberoylanilide hydroxamic acid (SAHA; preparation described).

L38 ANSWER 9 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:943096 HCAPLUS

DOCUMENT NUMBER: 141:33401

TITLE: Histone deacetylase inhibitors induce growth suppression and cell death in human rhabdomyosarcoma in vitro

AUTHOR(S): Kutko, Martha C.; Glick, Richard D.; Butler, Lisa M.; Coffey, Dennis C.; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.; LaQuaglia, Michael P.

CORPORATE SOURCE: Department of Pediatrics, Sloan Kettering Institute and Memorial Sloan Kettering Cancer Center, New York, NY, USA

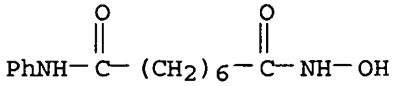
SOURCE: Clinical Cancer Research (2003), 9(15),

5749-5755
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A group of histone deacetylase inhibitors has been shown to be effective in suppressing the growth of a variety of transformed cell lines in vitro and in vivo. The effects of two of these agents, suberoylanilide hydroxamic acid (SAHA) and suberoyl-3-aminopyridineamide hydroxamic acid (pyroxamide), were investigated for their growth-suppressive effects on rhabdomyosarcoma (RMS) cells. Dose-response expts. of two RMS cell lines, RD (embryonal) and RH30B (alveolar), were performed with SAHA (0.25-3.0 μM) and pyroxamide (1.25-20.0 μM). Both agents caused a dose-dependent decrease in viable cell number and an increase in percentage of dead cells over time. Exposure of the RMS cells to SAHA and pyroxamide resulted in an accumulation of acetylated histones with increasing doses by Western blot anal. Addnl., there was an induction of p21/WAF1 at 15 and 24 h when the cells were cultured with SAHA (2.0 μM) or pyroxamide (20.0 μM), concns. that were tested because they successfully induced inhibition of cell growth and initiated cell death in both RMS cell lines. An increase in nuclei with hypodiploid or sub-G1 fraction was found by flow cytometry with increasing doses of both SAHA (0.25-3.0 μM) and pyroxamide (1.25-20.0 μM) over time. This finding is consistent with DNA fragmentation and cell death by apoptosis. SAHA and pyroxamide induce growth suppression and cell death in human RMS in vitro. Accumulation of acetylated histones and induction of p21/WAF1 expression are observed in cells exposed to either agent.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors induce growth suppression and cell death in human rhabdomyosarcoma in vitro)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 10 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:803900 HCAPLUS
DOCUMENT NUMBER: 140:56457
TITLE: Ring A-seco mosquito larvicidal limonoids from Turraea wakefieldii
AUTHOR(S): Ndung'u, Mary; Hassanali, Ahmed; Hooper, Antony M.; Chhabra, Sumesh; Miller, Thomas A.; Paul, Rowena L.; Torto, Baldwyn
CORPORATE SOURCE: International Centre of Insect Physiology and Ecology (ICIPE), Nairobi, Kenya
SOURCE: Phytochemistry (Elsevier) (2003), 64(4), 817-823
CODEN: PYTCAS; ISSN: 0031-9422

PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Five novel limonoids, 1-5, were isolated from the root bark of Turraea wakefieldii and were characterized as tecleaninoid derivs. This is the first report of the natural occurrence of tecleanin-type limonoids with a five-membered-ring A-seco structure for which we propose the name neotecleanins. The relative stereochem. structures of compds. 1-5 were established on the basis of NMR spectroscopy. The absolute stereochem. structure of 5 was confirmed by X-ray diffraction methods. In mosquito larvicidal assays, compds. 1, 2 and 4 showed dose-dependent larvicidal activity against larvae of Anopheles gambiae s.s.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 11 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:595088 HCAPLUS
DOCUMENT NUMBER: 140:69973
TITLE: Histone deacetylases
AUTHOR(S): Marks, Paul A.; Miller, Thomas; Richon, Victoria M.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, NY, USA
SOURCE: Current Opinion in Pharmacology (2003), 3(4), 344-351
CODEN: COPUBK; ISSN: 1471-4892
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Post-translational modification of the histones of chromatin has a fundamental role in regulating gene expression. Enzymes involved in these epigenetic events include histone deacetylases (class I and class II), which can be inhibited by a structurally diverse group of small mols. These histone deacetylase inhibitors induce growth arrest, differentiation and/or apoptosis of cancer cells in vitro and in vivo. Results of clin. trials with several of these agents have indicated that they are well tolerated at doses that have antitumor activity.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

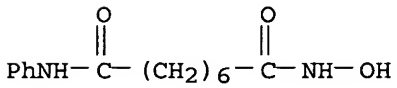
L38 ANSWER 12 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:405492 HCAPLUS
DOCUMENT NUMBER: 139:115446
TITLE: Molecular sequelae of histone deacetylase inhibition in human malignant B cells
AUTHOR(S): Mitsiades, Nicholas; Mitsiades, Constantine S.; Richardson, Paul G.; McMullan, Ciaran; Poulaki, Vassiliki; Fanourakis, Galinos; Schlossman, Robert; Chauhan, Dharminder; Munshi, Nikhil C.; Hideshima, Teru; Richon, Victoria M.; Marks, Paul A.; Anderson, Kenneth C.
CORPORATE SOURCE: Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Blood (2003), 101(10), 4055-4062
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone acetylation modulates gene expression, cellular differentiation,

and survival and is regulated by the opposing activities of histone acetyltransferases (HATs) and histone deacetylases (HDACs). HDAC inhibition results in accumulation of acetylated nucleosomal histones and induces differentiation and/or apoptosis in transformed cells. In this study, we characterized the effect of suberoylanilide hydroxamic acid (SAHA), the prototype of a series of hydroxamic acid-based HDAC inhibitors, in cell lines and patient cells from B-cell malignancies, including multiple myeloma (MM) and related disorders. SAHA induced apoptosis in all tumor cells tested, with increased p21 and p53 protein levels and dephosphorylation of Rb. We also detected cleavage of Bid, suggesting a role for Bcl-2 family members in regulation of SAHA-induced cell death. Transfection of Bcl-2 cDNA into MM.1S cells completely abrogated SAHA-induced apoptosis, confirming its protective role. SAHA did not induce cleavage of caspase-8, -9, or -3 in MM.1S cells during the early phase of apoptosis, and the pan-caspase inhibitor ZVAD-FMK did not protect against SAHA. Conversely, poly(ADP)ribose polymerase (PARP) was cleaved in a pattern indicative of calpain activation, and the calpain inhibitor calpeptin abrogated SAHA-induced cell death. Importantly, SAHA sensitized MM.1S cells to death receptor-mediated apoptosis and inhibited the secretion of interleukin 6 (IL-6) induced in bone marrow stromal cells (BMSCs) by binding of MM cells, suggesting that it can overcome cell adhesion-mediated drug resistance. Our studies delineate the mechanisms whereby HDAC inhibitors mediate anti-MM activity and overcome drug resistance in the BM milieu and provide the framework for clin. evaluation of SAHA, which is bioavailable, well tolerated, and bioactive after oral administration, to improve patient outcome.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study) (histone deacetylase inhibitor; authors characterized the effect of suberoylanilide hydroxamic acid (SAHA) in cell lines and patient cells from B-cell malignancies, including multiple myeloma (MM) and related disorders)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 13 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:314976 HCAPLUS

DOCUMENT NUMBER: 139:159591

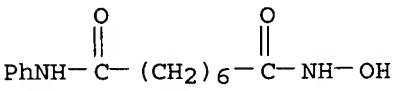
TITLE: Cotreatment with the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) enhances imatinib-induced apoptosis of Bcr-Abl-positive human acute leukemia cells

AUTHOR(S): Nimmanapalli, Ramadevi; Fuino, Lianne; Stobaugh, Corinne; Richon, Victoria; Bhalla, Kapil

CORPORATE SOURCE: Department of Interdisciplinary Oncology, Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, USA

SOURCE: Blood (2003), 101(8), 3236-3239

CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here we demonstrate that treatment with SAHA (suberoylanilide hydroxamic acid), a known inhibitor of histone deacetylases (HDACs), alone induced p21 and/or p27 expressions but decreased the mRNA and protein levels of Bcr-Abl, which was associated with apoptosis of Bcr-Abl-expressing K562 and LAMA-84 cells. Co-treatment with SAHA and imatinib (Gleevec) caused more down-regulation of the levels and auto-tyrosine phosphorylation of Bcr-Abl and apoptosis of these cell types, as compared with treatment with either agent alone (P <.05). This finding was also associated with a greater decline in the levels of phospho-AKT and Bcl-xL. Significantly, treatment with SAHA also down-regulated Bcr-Abl levels and induced apoptosis of CD34+ leukemia blast progenitor cells derived from patients who had developed progressive blast crisis (BC) of chronic myelocytic leukemia (CML) while receiving therapy with imatinib. Taken together, these findings indicate that cotreatment with SAHA enhances the cytotoxic effects of imatinib and may have activity against imatinib-refractory CML-BC.
IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cotreatment with the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) enhances imatinib-induced apoptosis of Bcr-Abl-pos. human acute leukemia cells)
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 14 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:184072 HCAPLUS
TITLE: SAHA-derived inhibitors of histone deacetylase
AUTHOR(S): Belvedere, Sandro; Zhou, Wen; Witter, David; Yan, Jiaming; Chen, Wei; Secrist, J. Paul; Richon, Victoria; Miller, Thomas
CORPORATE SOURCE: Aton Pharma Inc., Tarrytown, NY, 10591, USA
SOURCE: Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), MEDI-102. American Chemical Society: Washington, D. C.
CODEN: 69DSA4
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Histone deacetylases (HDACs) are a family of metalloenzymes that catalyze the removal of acetyl groups from lysines on histone proteins and play a major role in the regulation of chromatin structure. HDAC inhibitors have been shown to induce transcriptional activation, cell differentiation and

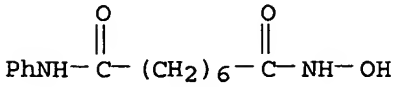
growth inhibition. Based on the structure of our lead agent SAHA , which is currently undergoing clin. trials, we have synthesized several highly potent HDAC inhibitors. Here we present the design, synthesis and structure-activity relationship of SAHA derived inhibitors of HDAC.

L38 ANSWER 15 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:155835 HCAPLUS
DOCUMENT NUMBER: 139:63206
TITLE: Suberoylanilide hydroxamic acid, a histone deacetylase inhibitor, ameliorates motor deficits in a mouse model of Huntington's disease
AUTHOR(S): Hockly, Emma; Richon, Victoria M.; Woodman, Benjamin; Smith, Donna L.; Zhou, Xianbo; Rosa, Eddie; Sathasivam, Kirupa; Ghazi-Noori, Shabnam; Mahal, Amarbirpal; Lowden, Philip A. S.; Steffan, Joan S.; Marsh, J. Lawrence; Thompson, Leslie M.; Lewis, Cathryn M.; Marks, Paul A.; Bates, Gillian P.
CORPORATE SOURCE: Medical and Molecular Genetics, Guy's, King's and St. Thomas' School of Medicine, King's College London, Guy's Hospital, London, SE1 9RT, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(4), 2041-2046
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

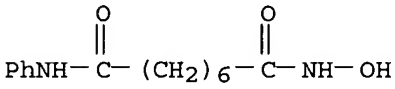
AB Huntington's disease (HD) is an inherited, progressive neurol. disorder that is caused by a CAG/polyglutamine repeat expansion and for which there is no effective therapy. Recent evidence indicates that transcriptional dysregulation may contribute to the mol. pathogenesis of this disease. Supporting this view, administration of histone deacetylase (HDAC) inhibitors has been shown to rescue lethality and photoreceptor neurodegeneration in a Drosophila model of polyglutamine disease. To further explore the therapeutic potential of HDAC inhibitors, we have conducted preclin. trials with suberoylanilide hydroxamic acid (SAHA), a potent HDAC inhibitor, in the R6/2 HD mouse model. We show that SAHA crosses the blood-brain barrier and increases histone acetylation in the brain. We found that SAHA could be administered orally in drinking water when complexed with cyclodextrins. SAHA dramatically improved the motor impairment in R6/2 mice, clearly validating the pursuit of this class of compds. as HD therapeutics.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid, histone deacetylase inhibitor, ameliorates motor deficits in mouse model of Huntington's disease)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



IT 149647-78-9D, Suberoylanilide hydroxamic acid, complex with cyclodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid -cyclodextrin complex as an aqueous solution for oral administration in the treatment of Huntington's disease)
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 16 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977966 HCAPLUS
DOCUMENT NUMBER: 138:51918
TITLE: Human histone deacetylase gene HDAC9 polypeptides and polynucleotides and uses thereof
INVENTOR(S): Richon, Victoria; Zhou, Xianbo; Rifkind, Richard A.; Marks, Paul A.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002102984	A2	20021227	WO 2002-US19051		20020614 <--
WO 2002102984	A3	20031113			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2465075	AA	20021227	CA 2002-2465075		20020614 <--
US 2003059812	A1	20030327	US 2002-173539		20020614
US 7063973	B2	20060620			
EP 1409661	A2	20040421	EP 2002-756203		20020614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004532647	T2	20041028	JP 2003-506439		20020614
US 2006030019	A1	20060209	US 2005-202268		20050810
PRIORITY APPLN. INFO.:			US 2001-298173P	P	20010614
			US 2001-311686P	P	20010810
			US 2001-316995P	P	20010904
			US 2002-173539	A3	20020614

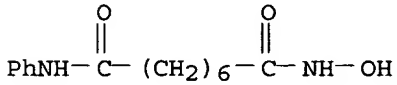
WO 2002-US19051 W 20020614

AB The invention claims cDNA and polypeptide sequences for histone deacetylases HDAC9, HDAC9a, HDAC9(ΔNLS), HDAC9a(ΔNLS), and histone deacetylase-related protein HDRP(ΔNLS) and isolated nucleic acid mols. encoding those polypeptides. The invention further claims vectors containing HDAC9, HDAC9a, HDAC9(ΔNLS), HDAC9a(ΔNLS), and HDRP(ΔNLS) nucleic acid sequences, cells containing those vectors, and antibodies which specifically bind the claimed polypeptides. Recombinant HDAC9 and HDRP nucleic acids and proteins may be used in methods for identifying HDAC enzyme activators and inhibitors and for identifying effectors of HDAC or HDRP gene expression. The invention also claims methods for identifying compds. which affect transcriptional regulation by histone deacetylase HDAC9 and related proteins. The invention claims use of HDAC9 and HDRP nucleic acids and polypeptides in methods for diagnosis and treatment of cell proliferation diseases, apoptotic diseases, or cell differentiation diseases. Examples of the invention include genomic organization of gene HDAC9, histone deacetylase activity of HDAC9 and HDAC9a isoenzymes, and HDAC9-dependent repression of transcription factor MEF2-mediated transcription. Gene HDAC9 was identified by sequence homol. of a translated open reading frame to the histone deacetylase domain of HDAC4. The gene is located on human chromosome 7 by database anal. and contains 26 exons. Exons 1-12 encode a non-catalytic domain and exons 14-21 encode the histone deacetylase catalytic domain. Cloning and sequence analyses of cDNAs and genomic DNA identified six isoforms produced by alternative splicing. These isoforms are designated HDAC9, HDAC9a, HDRP, HDRP(ΔNLS), HDAC9(ΔNLS), and HDAC9a(ΔNLS). Histone deacetylases HDAC9 and HDAC9a differ by 132 amino acids at the C-terminus, HDAC9 contains 1011 amino acids and HDAC9a contains 879 amino acids. The HDRP isoform contains 590 amino acids encoded by exons at the 5' end of gene HDAC9 and lacks the HDAC catalytic domain. Exon 7 of gene HDAC9 contains a nuclear localization signal and is alternatively spliced in HDRP, HDAC9 and/or HDAC9a to produce HDRP(ΔNLS), HDAC9(ΔNLS), and HDAC9a(ΔNLS).

IT 149647-78-9, SAHA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HDAC9 inhibitor; human histone deacetylase gene HDAC9 polypeptides and polynucleotides and uses thereof)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



L38 ANSWER 17 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:832536 HCAPLUS
DOCUMENT NUMBER: 137:306048
TITLE: Benzyl ester compositions for controlling populations of pest microorganisms
INVENTOR(S): Emerson, Ralph; Miller, Thomas
PATENT ASSIGNEE(S): Banks Group, LLC, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085115	A2	20021031	WO 2001-US49461	20011023 <--
WO 2002085115	A3	20030417		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2001-US49461 20011023

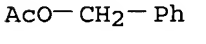
OTHER SOURCE(S): MARPAT 137:306048

AB Compns. for controlling pest populations of protists, protist-like organisms, water molds, algae, cyanobacteria, mosses, liverworts, hornworts, and combinations thereof on plants, livestock and pet animals contains one or more carboxy ester compds. which comprise aromatic acids, aliphatic acids, and/or salicylate derivs.

IT 140-11-4, Benzyl acetate
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(compns. for controlling pest microorganisms containing)

RN 140-11-4 HCAPLUS

CN Acetic acid, phenylmethyl ester (9CI) (CA INDEX NAME)



L38 ANSWER 18 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:711938 HCAPLUS

DOCUMENT NUMBER: 138:280808

TITLE: The histone deacetylase inhibitor SAHA arrests cancer cell growth, up-regulates thioredoxin-binding protein-2, and down-regulates thioredoxin

AUTHOR(S): Butler, Lisa M.; Zhou, Xianbo; Xu, Wei-Sheng; Scher, Howard I.; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.

CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(18), 11700-11705
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

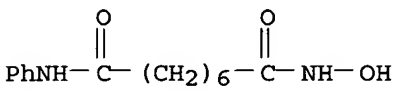
AB Suberoylanilide hydroxamic acid (SAHA) is a potent inhibitor of histone deacetylases (HDACs) that causes growth arrest, differentiation, and/or apoptosis of many tumor types in vitro and in vivo. SAHA is in clin. trials for the treatment of cancer. HDAC inhibitors induce the expression of less than 2% of genes in cultured cells. In this study we show that SAHA induces the expression of vitamin D-upregulated protein

1/thioredoxin-binding protein-2 (TBP-2) in transformed cells. As the expression of TBP-2 mRNA is increased, the expression of a second gene, thioredoxin, is decreased. In transient transfection assays, HDAC inhibitors induce TBP-2 promoter constructs, and this induction requires an NF-Y binding site. We report here that TBP-2 expression is reduced in human primary breast and colon tumors compared with adjacent tissue. These results support a model in which the expression of a subset of genes (i.e., including TBP-2) is repressed in transformed cells, leading to a block in differentiation, and culture of transformed cells with SAHA causes re-expression of these genes, leading to induction of growth arrest, differentiation, and/or apoptosis.

IT 149647-78-9
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of antitumor action of histone deacetylase inhibitor suberoylanilide hydroxamic acid)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 19 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:618078 HCAPLUS

TITLE: Histone deacetylase inhibitors and the treatment of cancers

AUTHOR(S): Rifkind, Richard A.; Richon, Victoria; Breslow, Ronald; Marks, Paul A.

CORPORATE SOURCE: The Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-226. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Based upon a strategy of searching for increasingly potent inducers of cancer cell differentiation cessation of proliferation, and apoptosis, which started with the observation that di-Me sulfoxide, at relatively high molar concentration(250 mM), had such properties, a series of increasingly potent hybrid polar compds. have been synthesized, and the most potent examples of this series have been found to be inhibitors of class I, II, and III histone deacetylases (HDACs). Structure/function anal. combined with x-ray crystallog. studies of the enzyme indicate that the chemical inhibitors such as suberoyl-analide hydroxamic acid (SAHA; effective in vitro at low micromolar concns.)are lysine analogs which insert within the protein's catalytic cleft, and coordinate with the zinc atoms found at the base of that cleft, thereby blocking the activity of the enzyme on its natural substrate, the N-terminal lysines of histone. The net effect measurable as a consequence of this inhibition is the hyperacetylation of histone N-terminal lysines and, apparently, a phys. reorganization of nucleosomal structure. The mol. basis for the selectivity of this effect on gene transcription remains obscure but a

role for other epigenetic factors, such as histone and/or DNA methylation, remains an important speculation. SAHA and a 2nd HDAC-inhibitor hydroxamic acid, pyroxamide, have recently entered clin. trials; accumulation of acetylated histone can be detected in the peripheral blood mononuclear cells and in tumor biopsies obtained from patients receiving SAHA. Phase I studies with i.v. administered SAHA have revealed that it is extremely well tolerated without significant side-effects up to and beyond the dose apparently needed to achieve radiol. measurable tumor regression and disease stabilization. A parallel phase I study of orally formulated and administered SAHA demonstrates oral bioavailability and evidence of efficacy without apparent toxicity.

L38 ANSWER 20 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:599943 HCAPLUS
DOCUMENT NUMBER: 138:162759
TITLE: Histone deacetylases and cancer: causes and therapies
AUTHOR(S): Marks, Paul A.; Rifkind, Richard A.; Richon, Victoria M.; Breslow, Ronald; Miller, Thomas; Kelly, William K.
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Nature Reviews Cancer (2001), 1(3), 194-202
CODEN: NRCAC4; ISSN: 1474-175X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Together, histone acetyltransferases and histone deacetylases (HDACs) determine the acetylation status of histones. This acetylation affects the regulation of gene expression, and inhibitors of HDACs have been found to cause growth arrest, differentiation and/or apoptosis of many tumors cells by altering the transcription of a small number of genes. HDAC inhibitors are proving to be an exciting therapeutic approach to cancer.
REFERENCE COUNT: 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 21 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:869541 HCAPLUS
DOCUMENT NUMBER: 136:132808
TITLE: Role of calcium homeostasis in gastric mucosal injury and protection
AUTHOR(S): Miller, Thomas A.; Kokoska, Evan R.; Smith, Gregory S.; Banan, Ali
CORPORATE SOURCE: Department of Surgery, Medical College of Virginia at Virginia, Commonwealth University, Richmond, VA, 23298, USA
SOURCE: Life Sciences (2001), 69(25/26), 3091-3102
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a human gastric mucosal cell line, known as AGS cells, we determined the role that perturbations in intracellular Ca2+ concentration [Ca2+]i might play in cellular injury induced by various damaging agents. For deoxycholate (CD) and ethanol (EtOH) induced damage, a concentration related increase in [Ca2+]i was noted that preceded and closely paralleled the magnitude of injury. Thus, the higher the concentration of DC or EtOH, the more profound were the changes in [Ca2+]i and the resultant degree of cellular injury.

Pretreatment with a low concentration of DC (50 μM; called a mild irritant) that was not damaging by itself attenuated injury induced by a damaging concentration (i.e. 250 μM) of DC, and appeared to elicit this protective action through mechanisms that resisted intracellular Ca2+ accumulation. Addnl. studies indicated that the mechanism of aspirin damage may be similar and that other protective agents such as prostaglandins and growth factors appear to mediate their protective properties through prevention of intracellular Ca2+ alterations. We propose that agents that prevent mucosal injury mediate this activity through a cellular response (involving active Ca2+ efflux) that subsequently provides a protective action by limiting the magnitude of intracellular Ca2+ accumulation.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(perturbations in intracellular Ca2+ concentration in cellular injury induced
by various damaging agents in human gastric mucosal cells)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 22 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:185885 HCAPLUS
DOCUMENT NUMBER: 134:237397
TITLE: Preparation of alkanoic acid derivatives as novel class of cytodifferentiating agents and histone deacetylase inhibitors, and methods of use thereof
INVENTOR(S): Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard A.; Breslow, Ronald; Belvedere, Sandro; Gershell, Leland; Miller, Thomas A.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA; Trustees of Columbia University in the City of New York
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018171	A2	20010315	WO 2000-US23232	20000824 <--
WO 2001018171	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383999	AA	20010315	CA 2000-2383999	20000824 <--
AU 2000069327	A5	20010410	AU 2000-69327	20000824 <--

EP 1231919	A2	20020821	EP 2000-957757		20000824 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
BR 2000014254	A	20020827	BR 2000-14254		20000824 <--
US 6511990	B1	20030128	US 2000-645430		20000824 <--
JP 2003509343	T2	20030311	JP 2001-522383		20000824
NZ 517613	A	20040130	NZ 2000-517613		20000824
ZA 2002001544	A	20021010	ZA 2002-1544		20020225 <--
US 2004002506	A1	20040101	US 2002-281875		20021025
AU 2005205805	A1	20050929	AU 2005-205805		20050902
PRIORITY APPLN. INFO.:			US 1999-152755P	P	19990908
			US 2000-208688P	P	20000601
			AU 2000-69327	A3	20000824
			US 2000-645430	A1	20000824
			WO 2000-US23232	W	20000824

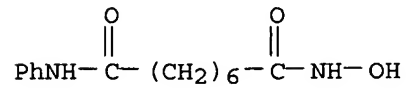
OTHER SOURCE(S): MARPAT 134:237397

AB The present invention provides the compound having formula R1NHCOCH(AR2)(CH2)nCONHOH (wherein each of R1 and R2 is, substituted or unsubstituted, aryl, cycloalkyl, cycloalkylamino, naphtha, pyridineamino, piperidino, tert-Bu, aryloxy, arylalkyloxy, or pyridine group; wherein A is an amido moiety, O, S, NH, or CH2; and wherein n is an integer from 3 to 8). The present invention also provides a method of selectively inducing growth arrest, terminal differentiation and/or apoptosis of neoplastic cells and thereby inhibiting proliferation of such cells. Moreover, the present invention provides a method of treating a patient having a tumor characterized by proliferation of neoplastic cells. Lastly, the present invention provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically acceptable amount of the compound above. Thus, N-benzoyl-L-α-aminosuberateanilide, i.e. PhCO-Asu-NHPh, was condensed with tert-butyldiphenylsilyloxyamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH2Cl2 at room temperature for 12 h, followed by deprotection with 5% CF3CO2H in CH2Cl2 for 1.5 h to give PhCO-Asu(NHOH)-NHPh (I). I and PhCH2O2C-Asu(NHOH)-NHR (R = quinolin-8-yl) showed activity of murine erythroleukemia cell (MEL) differentiation at 200 and 40 nM, resp., and inhibited histone deacetylase (HDAC) with ID50 of 1 and <10 nM, resp.

IT 149647-78-9P 149648-28-2P 329966-65-6P
329966-66-7P 329966-67-8P 329966-68-9P
329966-69-0P 329966-81-6P 329966-82-7P
329966-85-0P 329966-91-8P 329966-92-9P
329966-97-4P 329966-98-5P 329967-00-2P
329967-01-3P 329967-02-4P 329967-03-5P
329967-19-3P 329967-32-0P 329967-33-1P
329967-35-3P 329967-37-5P 329967-38-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkanoic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)

RN 149647-78-9 HCAPLUS

CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



RN 149648-28-2 HCAPLUS

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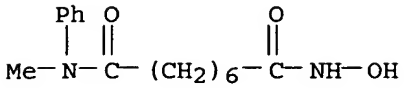
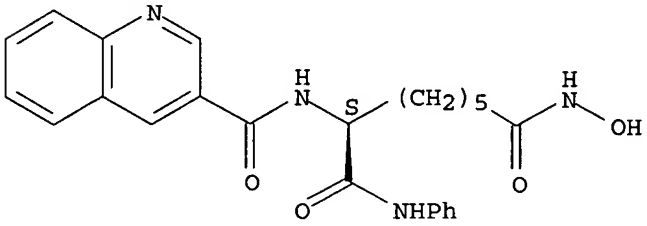


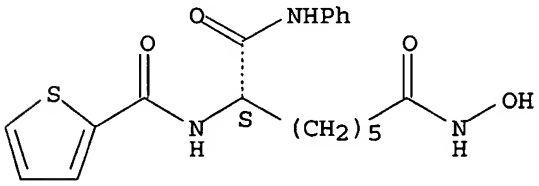
RN 329966-65-6 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(3-quinolinylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

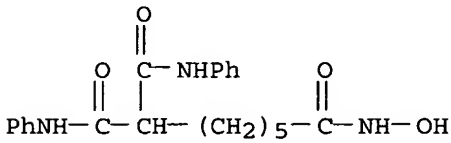


RN 329966-66-7 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(2-thienylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

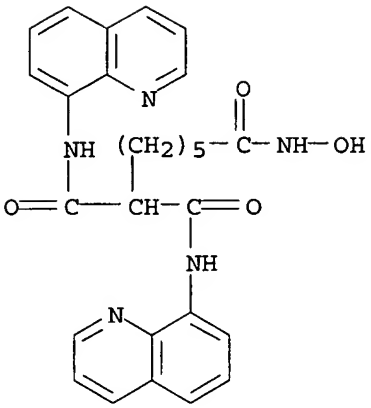
Absolute stereochemistry.



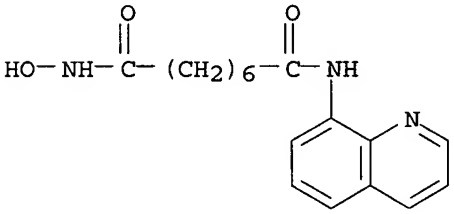
RN 329966-67-8 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-diphenyl- (9CI) (CA INDEX NAME)



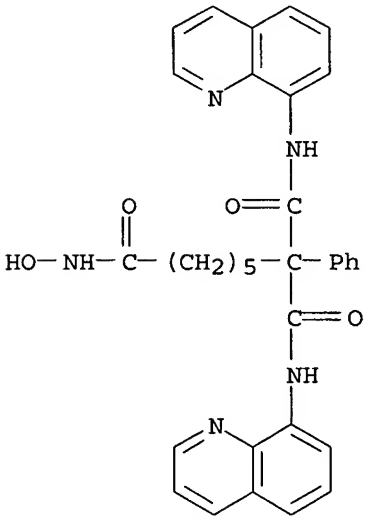
RN 329966-68-9 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-8-quinolinyl- (9CI) (CA INDEX NAME)



RN 329966-69-0 HCAPLUS
CN Octanediamide, N-hydroxy-N'-8-quinolinyl- (9CI) (CA INDEX NAME)

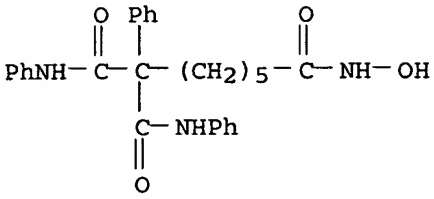


RN 329966-81-6 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-1-phenyl-N1,N1'-di-8-quinolinyl- (9CI) (CA INDEX NAME)

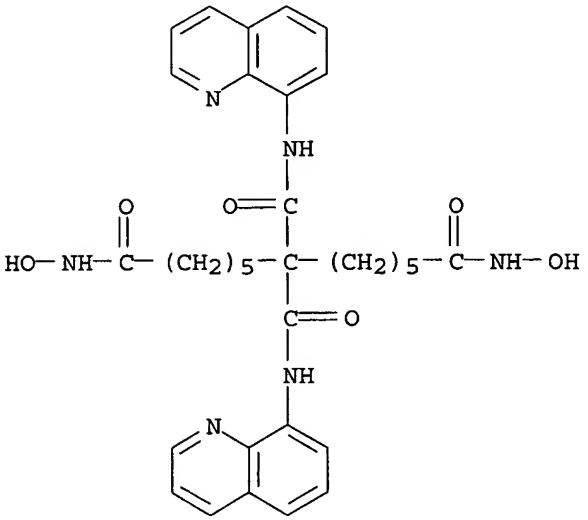


RN 329966-82-7 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1',1-triphenyl- (9CI) (CA

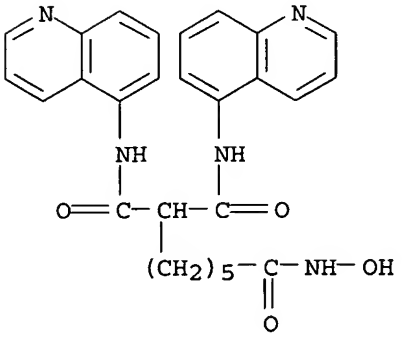
INDEX NAME)



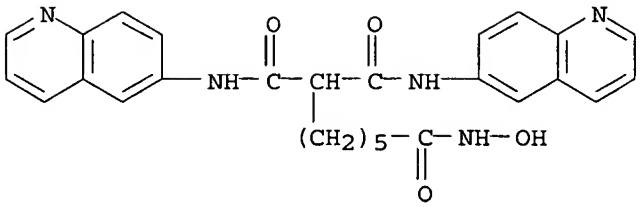
RN 329966-85-0 HCAPLUS
CN 1,6,6,11-Undecanetetracarboxamide, N1,N11-dihydroxy-N6,N6'-di-8-quinolinyl- (9CI) (CA INDEX NAME)



RN 329966-91-8 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-5-quinolinyl- (9CI) (CA INDEX NAME)

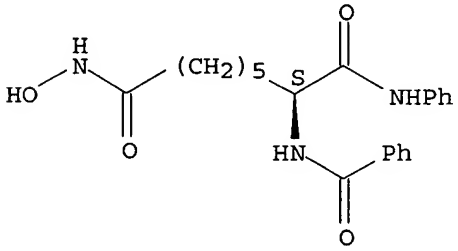


RN 329966-92-9 HCAPLUS
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-6-quinolinyl- (9CI) (CA INDEX NAME)



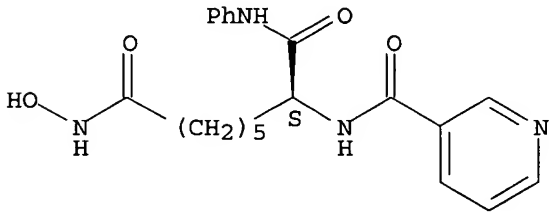
RN 329966-97-4 HCAPLUS
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



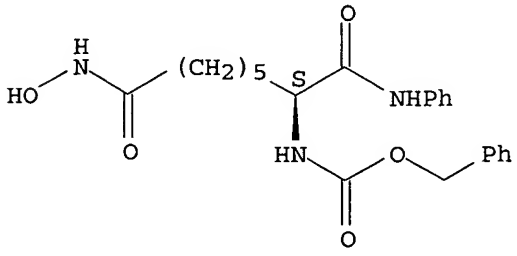
RN 329966-98-5 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(3-pyridinylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



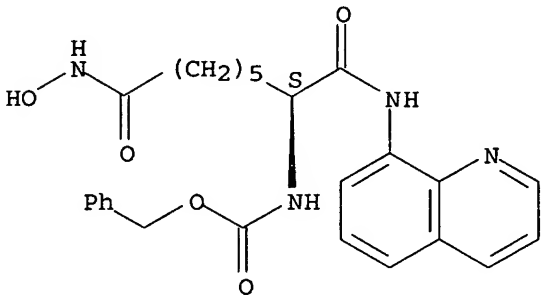
RN 329967-00-2 HCAPLUS
CN Carbamic acid, [(1S)-7-(hydroxyamino)-7-oxo-1-[(phenylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



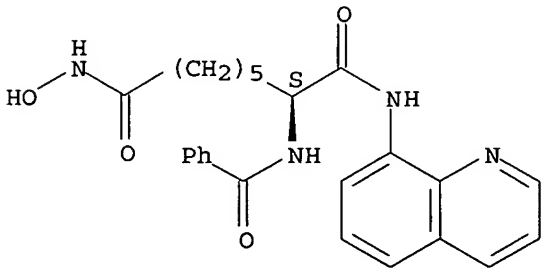
RN 329967-01-3 HCAPLUS
CN Carbamic acid, [(1S)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



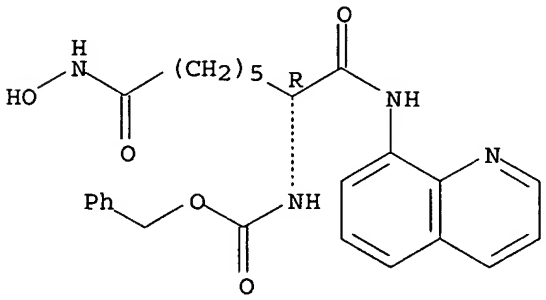
RN 329967-02-4 HCAPLUS
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-8-quinolinyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 329967-03-5 HCAPLUS
CN Carbamic acid, [(1R)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

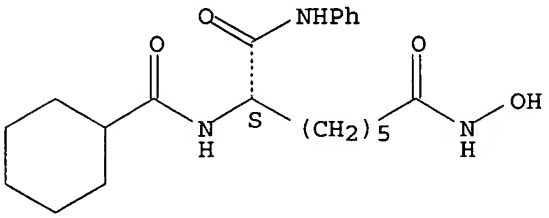
Absolute stereochemistry.



RN 329967-19-3 HCAPLUS

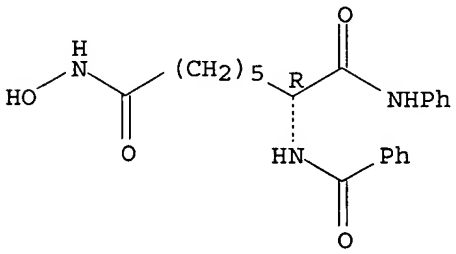
CN Octanediamide, 2-[(cyclohexylcarbonyl)amino]-N8-hydroxy-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

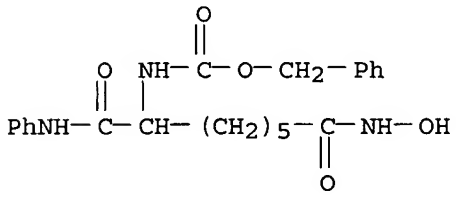


RN 329967-32-0 HCAPLUS
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-phenyl-, (2R)- (9CI) (CA INDEX NAME)

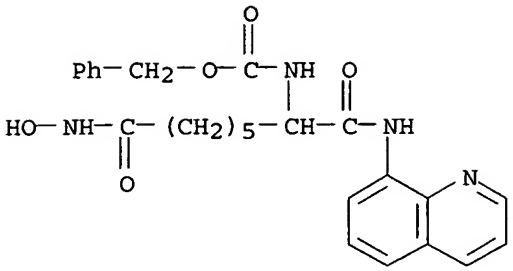
Absolute stereochemistry.



RN 329967-33-1 HCAPLUS
CN Carbamic acid, [7-(hydroxyamino)-7-oxo-1-[(phenylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

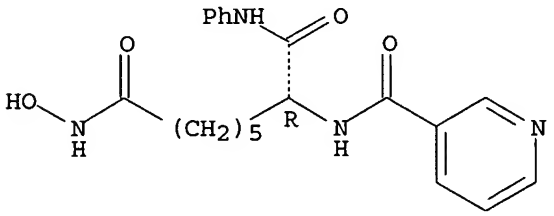


RN 329967-35-3 HCAPLUS
CN Carbamic acid, [7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



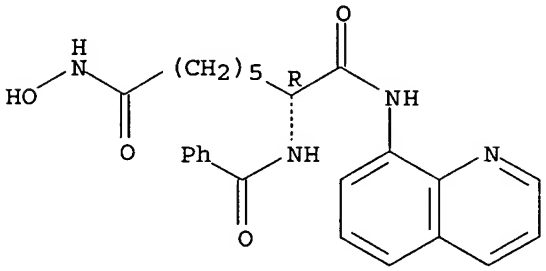
RN 329967-37-5 HCAPLUS
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(3-pyridinylcarbonyl)amino]-, (2R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



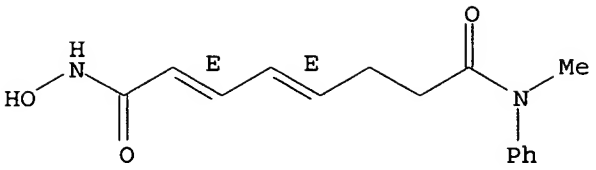
RN 329967-38-6 HCAPLUS
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-8-quinolinyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



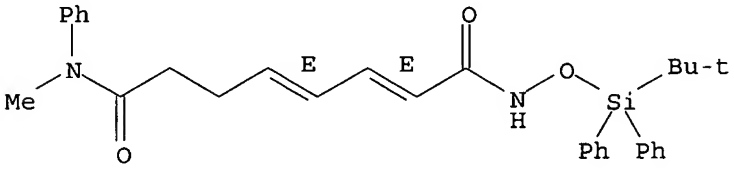
IT 329967-10-4P 329967-11-5P 329967-13-7P
329967-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkanoic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)
RN 329967-10-4 HCAPLUS
CN 2,4-Octadienediamide, N1-hydroxy-N8-methyl-N8-phenyl-, (2E,4E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



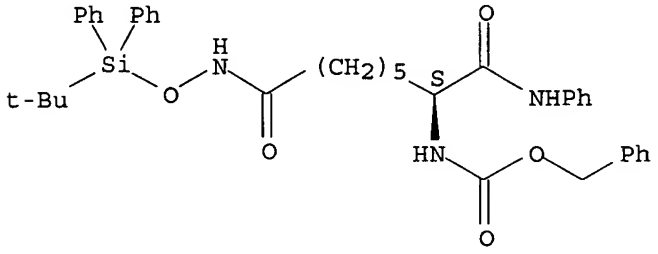
RN 329967-11-5 HCAPLUS
CN 2,4-Octadienediamide, N1-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-N8-methyl-N8-phenyl-, (2E,4E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



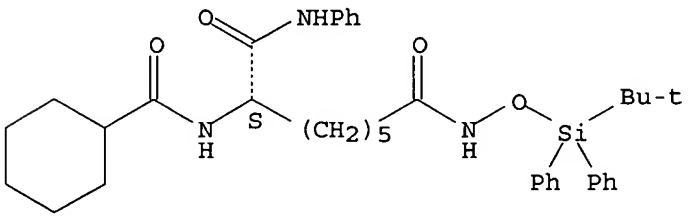
RN 329967-13-7 HCAPLUS
CN 11-Oxa-2,10-diaza-12-silatetradecanoic acid, 13,13-dimethyl-9-oxo-12,12-diphenyl-3-[(phenylamino)carbonyl]-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 329967-20-6 HCAPLUS
CN Octanediamide, 2-[(cyclohexylcarbonyl)amino]-N8-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-N1-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 23 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:185791 HCAPLUS

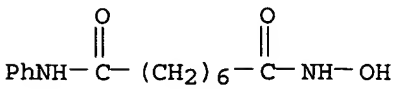
DOCUMENT NUMBER: 134:204354
TITLE: Crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors
INVENTOR(S): Pavletich, Nikola; Finnin, Michael; Donigian, Jill; Richon, Victoria; Rifkind, Richard A.; Marks, Paul A.; Breslow, Ronald
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA; Trustees of Columbia University in the City of New York
SOURCE: PCT Int. Appl., 329 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018045	A1	20010315	WO 2000-US24700	20000908 <--
WO 2001018045	C2	20021107		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2383885	AA	20010315	CA 2000-2383885	20000908 <--
EP 1212357	A1	20020612	EP 2000-968344	20000908 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2003518923	T2	20030617	JP 2001-522267	20000908
US 2003013176	A1	20030116	US 2002-95109	20020308 <--
PRIORITY APPLN. INFO.:			US 1999-152753P P	19990908
			WO 2000-US24700 W	20000908

AB The present invention provides three-dimensional structural information of the histone deacetylase-like protein (HDLP) from the hyperthermophilic bacterium Aquifex aeolicus. HDLP shares 35.2% amino acid sequence identity with human histone deacetylase (HDAC1). The double mutant C75S/C77S of HDLP is used to facilitate the determination of three-dimensional structure of HDLP bound to a zinc atom at its zinc atom-binding site. The present invention further provides three-dimensional structural information of HDLP double mutant bound by inhibitor mols. (e.g., trichostatin A or suberoyl anilide hydroxamic acid). The three-dimensional structural information of the present invention is useful to design, isolate and screen deacetylase inhibitor compds. capable of inhibiting HDLP, HDAC family members, and HDLP-related mols. The invention also relates to nucleic acids encoding a mutant HDLP which facilitates the determination of the three-dimensional structure of HDLP in the presence of a zinc atom.

IT 149647-78-9D, complex with deacetylase protein
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 24 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:786894 HCAPLUS
DOCUMENT NUMBER: 134:66596
TITLE: Cytoskeleton as a target for injury in damaged intestinal epithelium
AUTHOR(S): Miller, Thomas A.; Smith, Gregory S.; Banan, Ali; Kokoska, Evan R.
CORPORATE SOURCE: Theodore Cooper Surgical Research Institute, Department of Surgery, Saint Louis University Health Sciences Center, St. Louis, MO, 63104, USA
SOURCE: Microscopy Research and Technique (2000), 51(2), 149-155
CODEN: MRTEEO; ISSN: 1059-910X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This report summarizes the findings of a series of studies undertaken to discern the role of the cytoskeleton in intestinal injury and defense. Two established cell lines were used for these studies. IEC-6 cells (a rat intestinal cell line) were incubated in Eagle's minimal essential medium with and without 16,16 di-Me prostaglandin E2 (dmPGE2; 2.6 μM) for 15 min and subsequently incubated in medium containing 10% ethanol (EtOH). The effects on cell viability and the actin cytoskeleton were then determined Using a similar protocol, Caco-2 cells (a human colonic cell line) were employed to assess the microtubule cytoskeleton under these conditions. In both cell lines, EtOH extensively disrupted the cytoskeletal component being evaluated coincident with adversely affecting cell viability. Pretreatment with dmPGE2 increased cell viability and abolished the disruptive effects on both the actin and microtubule cytoskeleton in cells exposed to EtOH. Prior incubation with cytochalasin D, an actin disruptive agent, prevented the protective capabilities of dmPGE2 in IEC-6 cells challenged with EtOH. Phalloidin, an actin stabilizing agent, demonstrated similar effects to that of dmPGE2 by stabilizing the actin cytoskeleton and preserving cellular viability in IEC-6 cells in response to EtOH. In Caco-2 cells, taxol, a microtubule stabilizing agent, mimicked the effects of dmPGE2 by increasing cell viability in cells exposed to EtOH and enhancing microtubular integrity. In contrast, pretreatment with colchicine, an inhibitor of microtubule integrity, prevented the protective effects of dmPGE2. These findings support the hypothesis that the cytoskeleton may be a major target for injury in damaged intestinal epithelium, and that the protective action of dmPGE2 is orchestrated through preservation of this target.

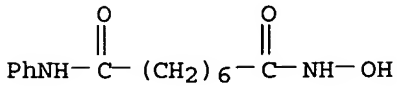
IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cytoskeleton involvement in ethanol-induced injury in damaged intestinal epithelium and in cytoprotection by prostaglandin)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 25 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:702583 HCAPLUS
DOCUMENT NUMBER: 134:272
TITLE: Suberoylanilide hydroxamic acid, an inhibitor of histone deacetylase, suppresses the growth of prostate cancer cells in vitro and in vivo
AUTHOR(S): Butler, Lisa M.; Agus, David B.; Scher, Howard I.; Higgins, Brian; Rose, Adam; Cordon-Cardo, Carlos; Thaler, Howard T.; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Cancer Research (2000), 60(18), 5165-5170
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Suberoylanilide hydroxamic acid (SAHA) is the prototype of a family of hybrid polar compds. that induce growth arrest in transformed cells and show promise for the treatment of cancer. SAHA induces differentiation and/or apoptosis in certain transformed cells in culture and is a potent inhibitor of histone deacetylases. In this study, we examined the effects of SAHA on the growth of human prostate cancer cells in culture and on the growth of the CWR22 human prostate xenograft in nude mice. SAHA suppressed the growth of the LNCaP, PC-3, and TSU-Pr1 cell lines at micromolar concns. (2.5-7.5 μM). SAHA induced dose-dependent cell death in the LNCaP cells. In mice with transplanted CWR22 human prostate tumors, SAHA (25, 50, and 100 mg/kg/day) caused significant suppression of tumor growth compared with mice receiving vehicle alone; treatment with 50 mg/kg/day resulted in a 97% reduction in the mean final tumor volume compared with controls. At this dose, there was no detectable toxicity as evaluated by weight gain and necropsy examination Increased accumulation of acetylated core histones was detected in the CWR22 tumors within 6 h of SAHA administration. SAHA induced prostate-specific antigen mRNA expression in CWR22 prostate cancer cells, resulting in higher levels of serum prostate-specific antigen than predicted from tumor volume alone. The results suggest that hydroxamic acid-based hybrid polar compds. inhibit prostate cancer cell growth and may be useful, relatively nontoxic agents for the treatment of prostate carcinoma.

IT 149647-78-9
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid suppresses the growth of prostate cancer cells in vitro and in vivo)
RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 26 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:595479 HCAPLUS
DOCUMENT NUMBER: 133:335091
TITLE: 5-HETE congeners as modulators of cell proliferation
AUTHOR(S): Miller, T. A.; Ghosh, J.; Myers, C. E.; Macdonald, T. L.
CORPORATE SOURCE: Department of Chemistry, University of Virginia, Charlottesville, VA, 22901, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(17), 1913-1916
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:335091
AB The synthesis and assessment of the mitogenic properties of 5-HETE congeners are reported. These studies represent an effort to develop a structure-activity profile for ligands of the 5-HETE/5-oxoETE G-protein coupled receptor(s). Many of these agents possess mitogenic activity that equals or exceeds that of racemic 5-HETE family constituents in prostate cancer cell lines.
IT 141-43-5, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(5-HETE congeners as modulators of cell proliferation)
RN 141-43-5 HCAPLUS
CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-OH$

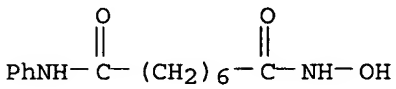
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 27 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:152114 HCAPLUS
DOCUMENT NUMBER: 133:53256
TITLE: Chemoprevention of carcinogen-induced mammary tumorigenesis by the hybrid polar cytodifferentiation agent, suberanilohydroxamic acid (SAHA)
AUTHOR(S): Cohen, Leonard A.; Amin, Shantu; Marks, Paul A.; Rifkind, Richard A.; Desai, Dhimant; Richon, Victoria M.
CORPORATE SOURCE: American Health Foundation, Valhalla, NY, 10595, USA
SOURCE: Anticancer Research (1999), 19(6B), 4999-5005
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hybrid Polar Cytodifferentiation (HPC) agents represent a novel class of anticancer compds. which act by inducing terminal differentiation and/or apoptosis rather than by cytotoxic action. Among these are HPC agents such as hexamethylenebis-acetamide (HMBA) and more potent 2nd generation hybrid/polar compds. such as suberanilohydroxamic acid (SAHA). As of the present, most studies on HPC agents have focused on cancers of the hematopoietic system rather than solid epithelial tumors. The objective of the present study therefore was to assess the chemopreventive action of these two related compds. in the N-methylnitrosourea (NMU)-induced rat mammary tumor model. Female Sprague-Dawley rats were

fed diets containing 450 and 900 ppm, SAHA and 1000 and 2000 ppm HMBA, starting one week prior to NMU administration and continued for a period of 18 wk. Mammary tumor development was monitored by palpation throughout the study, and at termination tumor incidence, number, multiplicity, latency and volume were determined Weight gain was measured biweekly throughout the study. The salient results were as follows: SAHA at 900 ppm reduced NMU-induced mammary tumor incidence by 40%, total tumors by 66%, mean tumor multiplicity by 43% and mean tumor volume by 78%, with no detectable toxic side effects. HMBA exerted no tumor inhibiting effects at either concentration This study represents the first demonstration that an HPC agent, namely SAHA, can inhibit the development of a chemical-induced, solid, epithelial tumor, at a relatively low dose (approx. 13 mg/rat/day) without untoward side effects.

IT 149647-78-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemoprevention of carcinogen-induced mammary tumorigenesis by hybrid polar cytodifferentiation agent, suberanilohydroxamic acid (SAHA))

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 28 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:56383 HCAPLUS
DOCUMENT NUMBER: 132:318836
TITLE: Role of Actin Cytoskeleton in Prostaglandin-Induced Protection against Ethanol in an Intestinal Epithelial Cell Line
AUTHOR(S): Banan, A.; Smith, G. S.; Kokoska, E. R.; Miller, T. A.
CORPORATE SOURCE: Theodore Cooper Surgical Research Institute, Department of Surgery, Saint Louis University Health Sciences Center, St. Louis, MO, 63104, USA
SOURCE: Journal of Surgical Research (2000), 88(2), 104-113
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandins (PGs) protect a variety of gastrointestinal cells against injury induced by ethanol and other noxious agents. This investigation attempted to discern the mechanism of cytoprotection as it relates to the relationship between actin and PGs in IEC-6 cells (a rat intestinal epithelial cell line). IEC-6 cells were incubated in Dulbecco's modified Eagle's medium ± 16,16-dimethylprostaglandin E2 (dmPG, 2.6 μM) for 15 min and subsequently incubated in medium containing 1, 2.5, 5, 7.5, and 10% ethanol (EtOH). Cells were then processed for immunocytochem. using FITC-phalloidin in order to stain the actin cytoskeleton, and cell viability was determined by trypan blue exclusion.

Quant. Western immunoblotting of fractioned G-actin (nonpolymd.; S1) and F-actin (polymerized; S2) was also carried out. EtOH concns. equal to and greater than 5% led to the collapse of the actin cytoskeleton as depicted by extensive disorganization and fragmentation. In addition, these same EtOH concns. significantly decreased the S2 fraction and increased the S1 pool of actin. Preincubation with dmPG prevented the collapse of the actin cytoskeleton, significantly increased the S2 polymerized fraction as determined by quant. immunoblotting, and increased cell viability in EtOH-treated cultures. Prior incubation with cytochalasin D, an actin-disruptive agent, not only reduced cell viability but also prevented the cytoprotective effects of dmPG. Phalloidin, an actin-stabilizing agent, had effects similar to that of dmPG as demonstrated by the stability of the actin cytoskeleton and increased cellular viability. Such findings indicate that PGs are important in the organization and stability of actin under in vitro conditions. These effects on actin may play an essential role in the mechanism of PG-induced cytoprotection. (c) 2000 Academic Press.

IT 64-17-5, Ethanol; biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(role of actin cytoskeleton in prostaglandin-induced protection against ethanol in intestinal epithelial cell line)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 29 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

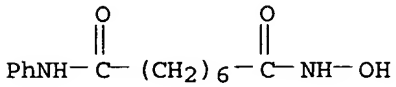
ACCESSION NUMBER: 2000:17291 HCAPLUS
DOCUMENT NUMBER: 132:202737
TITLE: Induction of apoptosis in U937 human leukemia cells by suberoylanilide hydroxamic acid (SAHA) proceeds through pathways that are regulated by Bcl-2/Bcl-XL, c-Jun, and p21CIP1, but independent of p53
AUTHOR(S): Vrana, J. A.; Decker, R. H.; Johnson, C. R.; Wang, Z.; Jarvis, W. D.; Richon, V. M.; Ehinger, M.; Fisher, P. B.; Grant, S.
CORPORATE SOURCE: Department of Medicine, Medical College of Virginia, Richmond, VA, 23298, USA
SOURCE: Oncogene (1999), 18(50), 7016-7025
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Determinants of differentiation and apoptosis in myelomonocytic leukemia cells (U937) exposed to the novel hybrid polar compound SAHA (suberoylanilide hydroxamic acid) have been examined In contrast to hexamethylenbisacetamide (HMBA), SAHA -related maturation was limited and accompanied by marked cytotoxicity. SAHA-mediated apoptosis occurred within the G0G1 and S phase populations, and was associated with decreased mitochondrial membrane potential, caspase-3 activation, PARP degradation, hypophosphorylation/cleavage of pRB, and down-regulation of c-Myc, c-Myb, and B-Myb. Enforced expression of Bcl-2 or Bcl-xL inhibited SAHA

-induced apoptosis, but only modestly potentiated differentiation. While SAHA induced the cyclin-dependent kinase inhibitor p21CIP1, antisense ablation of this CDKI increased, rather than decreased, SAHA-related lethality. In contrast, conditional expression of wild-type p53 failed to modify SAHA actions, but markedly potentiated HMBA-induced apoptosis. Finally, SAHA modestly increased expression/activation of the stress-activated protein kinase (SAPK/JNK); moreover, SAHA-related lethality was partially attenuated by a dominant-neg. c-Jun mutant protein (TAM67). SAHA did not stimulate mitogen-activated protein kinase (MAPK), nor was lethality diminished by the specific MEK/MAPK inhibitor PD98059. These findings indicate that SAHA potently induces apoptosis in human leukemia cells via a pathway that is p53-independent but at least partially regulated by Bcl-2/Bcl-xL, p21CIP1, and the c-Jun/AP-1 signaling cascade.

IT 149647-78-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of apoptosis in U937 human leukemia cells by suberoylanilide hydroxamic acid (SAHA) proceeds through pathways that are regulated by Bcl-2/Bcl-XL, c-Jun, and p21CIP1, but independent of p53)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

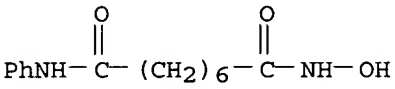
L38 ANSWER 30 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:596349 HCAPLUS
DOCUMENT NUMBER: 131:334011
TITLE: Structures of a histone deacetylase homologue bound to the TSA and SAHA inhibitors
AUTHOR(S): Finnin, Michael S.; Donigian, Jill R.; Cohen, Alona; Richon, Victoria M.; Rifkind, Richard A.; Marks, Paul A.; Breslow, Ronald; Pavletich, Nikola P.
CORPORATE SOURCE: Cellular Biochemistry and Biophsyics Program and Howard Hughes Medical Institute, Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Nature (London) (1999), 401(6749), 188-193
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Histone deacetylases (HDACs) mediate changes in nucleosome conformation and are important in the regulation of gene expression. HDACs are involved in cell-cycle progression and differentiation, and their deregulation is associated with several cancers. HDAC inhibitors, such as trichostatin A (TSA) and suberoylanilide hydroxamic acid (SAHA), have anti-tumor effects, as they can inhibit cell growth, induce terminal differentiation and prevent the formation of tumors in mice models, and they are effective in the

treatment of promyelocytic leukemia. Here we describe the structure of the histone deacetylase catalytic core, as revealed by the crystal structure of a homolog from the hyperthermophilic bacterium Aquifex aeolicus, that shares 35.2% identity with human HDAC1 over 375 residues, deacetylates histones in vitro and is inhibited by TSA and SAHA. The deacetylase, deacetylase-TSA and deacetylase-SAHA structures reveal an active site consisting of a tubular pocket, a zinc-binding site and two Asp-His charge-relay systems, and establish the mechanism of HDAC inhibition. The residues that make up the active site and contact the inhibitors are conserved across the HDAC family. These structures also suggest a mechanism for the deacetylation reaction and provide a framework for the further development of HDAC inhibitors as antitumor agents.

IT 149647-78-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(crystal structures of histone deacetylase homolog bound to trichostatin A and suberoylanilide hydroxamic acid)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 31 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:449817 HCAPLUS
DOCUMENT NUMBER: 131:224189
TITLE: Cloning of the cDNA encoding phenylalanyl tRNA synthetase regulatory α-subunit-like protein whose expression is down-regulated during differentiation
AUTHOR(S): Zhou, Xianbo; Richon, Victoria M.; Ngo, Lang; Rifkind, Richard A.; Marks, Paul A.
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center and Graduate School of Medical Sciences, Sloan-Kettering Institute, Cell Biology Program, Cornell University Medical School, New York, NY, USA
SOURCE: Gene (1999), 233(1-2), 13-19
CODEN: GENED6; ISSN: 0378-1119
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hybrid polar compds. (HPCs), such as suberoylanilide hydroxamic acid (SAHA), induce differentiation of transformed cells. Differential display of RNA was used to identify genes whose expression is changed during SAHA-induced differentiation of murine erythroleukemia (MEL) cells. One such cDNA was identified whose mRNA level decreased by 50% after 8 h of SAHA treatment as determined by Northern blot anal. The full-length cDNA (1944 bp in length) was cloned by sequencing of an EST clone and rapid amplification of 5' cDNA ends (5'-RACE). The predicted amino acid sequence is 589 amino acids and shares 45% identity with the yeast cytoplasmic phenylalanyl tRNA synthetase (PheRS) regulatory α-subunit. Human EST clones which share over 90% identity of

predicted amino acid sequence with this cDNA map to chromosome 2 near the paired box homeotic gene 3 (PAX3) locus, a region syntenic to mouse chromosome 1. This is the first report of the cloning of the full-length cDNA for the murine PheRS regulatory α-subunit-like protein. The level of PheRS α-subunit-like mRNA is regulated during differentiation but not during cell cycle progression.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 32 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:293733 HCAPLUS
DOCUMENT NUMBER: 131:125827
TITLE: Prostaglandins protect human intestinal cells against ethanol injury by stabilizing microtubules: Role of protein kinase C and enhanced calcium efflux
AUTHOR(S): Banan, A.; Smith, G. S.; Deshpande, Y.; Rieckenberg, C. L.; Kokoska, E. R.; Miller, T. A.
CORPORATE SOURCE: Theodore Cooper Surgical Research Institute, Department of Surgery, Saint Louis University Health Sciences Center, St. Louis, MO, 63104, USA
SOURCE: Digestive Diseases and Sciences (1999), 44(4), 697-707
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandins (PG) protect gastrointestinal cells against damage induced by ethanol (EtOH) and other noxious agents, a process termed cytoprotection. The present study investigated the relationships between microtubule (MT) stability, protein kinase C (PKC) activation, and calcium efflux as a possible mechanism of PG's protective action using a human colonic cell line (Caco-2) exposed to known damaging concns. of EtOH (7.5% and 10%). Preincubation of Caco-2 cells with 16,16-dimethyl-PGE2 (PG, 2.6 μM) significantly increased PKC activity in these cells. Pretreatment of Caco-2 cells with 50 μM OAG (a synthetic diacylglycerol and PKC activator) or 30 nM TPA (a direct PKC activator) prior to exposure to 7.5% or 10% EtOH for 5 min significantly reduced cell injury, as determined by trypan blue exclusion, and increased MT stability, as confirmed by confocal microscopy. Pretreatment of Caco-2 cells with 4 α-PDD (an inactive phorbol ester, 20 nM) failed to prevent cell injury and disruption of the MT cytoskeleton. Preincubation with staurosporine (a PKC inhibitor, 3 nM) abolished the protective effects of PG in cells exposed to 7.5% and 10% EtOH. Incubation of Caco-2 cells with A23187 (a Ca2+ ionophore), similar to 10% EtOH, caused a significant reduction in cell viability and MT stability. Preincubation with A23187 in combination with PG or OAG prior to subsequent exposure to EtOH significantly abolished the protective effects of PG or OAG pretreatment. Finally, pretreatment with OAG, TPA, or PG resulted in significant increases in calcium-45 efflux, which correlated with increased stability of the MT cytoskeleton. These data suggest that PG possesses direct protective effects against EtOH injury in Caco-2 cells and may act by stabilizing MT through the PKC signal transduction pathway and/or stimulation of calcium efflux from the cells.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(prostaglandins protect human intestinal cells against ethanol injury by stabilizing microtubules via protein kinase C and/or enhanced calcium efflux)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 33 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:273351 HCAPLUS
DOCUMENT NUMBER: 129:73341
TITLE: Characterization of nonequilibrium Al - Mo alloys formed by EB-PVD
AUTHOR(S): Sikora, E.; Shaw, B. A.; Miller, T.
CORPORATE SOURCE: Department of Engineering Science and Mechanics, The Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Proceedings - Electrochemical Society (1998), 97-26(Passivity and Its Breakdown), 654-664
CODEN: PESODO; ISSN: 0161-6374
PUBLISHER: Electrochemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nonequil. Al-Mo alloys produced by electron beam phys. vapor deposition (EB-PVD) were characterized by SEM, X-ray diffraction (XRD) and atomic force microscopy (AFM). Nonequil. Al-Mo alloys display high resistance against localized corrosion. In the range of Mo concns. evaluated in this study the corrosion performance of nonequil. Al-Mo alloys was a function of their morphol. rather than of molybdenum content in the alloy. Dense structures displayed the best corrosion resistance, whereas, the presence of microcrevices in columnar deposits substantially deteriorated corrosion resistance.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 34 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:245108 HCAPLUS
DOCUMENT NUMBER: 129:49880
TITLE: Cyclooxygenase inhibition attenuates cholecystokinin-induced gastroprotection
AUTHOR(S): Mercer, David W.; Smith, Gregory S.; Miller, Thomas A.
CORPORATE SOURCE: Department of Surgery, The University of Texas-Houston Medical School, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1998), 43(3), 468-475
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholecystokinin prevents gastric injury by an unknown mechanism. This study was conducted in conscious, fasted female rats to assess the role of endogenous prostaglandins as a potential protective mechanism for cholecystokinin-induced gastroprotection. I.v. administration of cholecystokinin (0.05-5 nmol/kg) dose-dependently reduced macroscopic injury to the glandular portion of the stomach caused by 1 mL of orally administered acidified ethanol (150 mM hydrochloric acid-50% ethanol), an effect corroborated by histol. anal. In time course studies, this protective action occurred as early as 10 min following cholecystokinin injection (5 nmol/kg i.v.), but was absent at 1 h.

Cyclooxygenase inhibition with either indomethacin (5 mg/kg i.p.) or aspirin (100 mg/kg i.p.) resulted in a partial reversal in cholecystokinin-induced gastroprotection, effects that were similar in magnitude. However, while indomethacin reduced gastric mucosal prostaglandin synthesis (enzyme-linked immunoassay) by 60%, aspirin almost totally abolished prostaglandin synthesis (95% reduction). Cholecystokinin (5 nmol/kg i.v.) did not significantly enhance gastric mucosal prostaglandin synthesis in the absence of cyclooxygenase inhibition. These data indicate that cholecystokinin requires the presence of endogenous prostaglandins to fully exert its gastroprotective actions. However, release of endogenous prostaglandins does not entirely explain the protective response, and addnl. factors likely participate in this action.

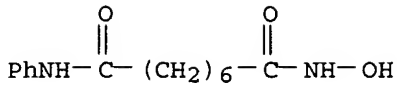
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 35 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:209144 HCAPLUS
DOCUMENT NUMBER: 128:316984
TITLE: A class of hybrid polar inducers of transformed cell differentiation inhibits histone deacetylases
AUTHOR(S): Richon, Vicotria M.; Emiliani, Stephane; Verdin, Eric; Webb, Yael; Breslow, Ronald; Rifkind, Richard A.; Marks, Paul A.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(6), 3003-3007
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hybrid polar compds. (HPCs) have been synthesized that induce terminal differentiation and/or apoptosis in various transformed cells. We have previously reported on the development of the second-generation HPCs suberoylanilide hydroxamic acid (SAHA) and m-carboxycinnamic acid bishydroxamide (CBHA) that are 2,000-fold more potent inducers on a molar basis than the prototype HPC hexamethylene bisacetamide (HMBA). Herein we report that CBHA and SAHA inhibit histone deacetylase 1 (HDAC1) and histone deacetylase 3 (HDAC3) activity in vitro. Treatment of cells in culture with SAHA results in a marked hyperacetylation of histone H4, but culture with HMBA does not. Murine erythroleukemia cells developed for resistance to SAHA are cross-resistant to trichostatin A, a known deacetylase inhibitor and differentiation inducer, but are not cross-resistant to HMBA. These studies show that the second-generation HPCs, unlike HMBA, are potent inhibitors of HDAC activity. In this sense, HMBA and the second-generation HPCs appear to induce differentiation by different pathways.

IT 149647-78-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hybrid polar inducers of transformed cell differentiation inhibits histone deacetylases)

RN 149647-78-9 HCAPLUS
CN Octanediamide, N-hydroxy-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 36 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:81987 HCAPLUS
DOCUMENT NUMBER: 128:201901
TITLE: Protection against ethanol injury by prostaglandin in a human intestinal cell line: role of microtubules
AUTHOR(S): Banan, A.; Smith, G. S.; Rieckenberg, C. L.; Kokoska, E. R.; Miller, T. A.
CORPORATE SOURCE: Theodore Copper Surgical Research Institute, Dep. of Surgery, Saint Louis University Medical Center, St. Louis, MO, 63104, USA
SOURCE: American Journal of Physiology (1998), 274(1, Pt. 1), G111-G121
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandins have been shown to protect the gastrointestinal (GI) epithelium from injury induced by various luminal insults independent of their known acid-inhibitory effects, a process termed "cytoprotection". The mechanism of this protective action remains unknown. The present investigation determined the role of microtubules (a major cytoskeletal component) in GI injury induced by EtOH and its prevention by 16,16-dimethylprostaglandin E2 (dmPGE2) using cells from a human colonic cell line known as Caco-2 cells. These cells were preincubated in Eagle's min. essential medium with and without dmPGE2 (2.6 μM) for 15 min and subsequently incubated in media containing 1, 2.5, 5, 7.5, and 10% EtOH. The effects on cell viability and tubulin (the major protein backbone of microtubules) were then determined EtOH concns. ≥2.5% extensively disrupted the microtubules as demonstrated by fragmentation, kinking, and perturbation of the microtubule organizer center. EtOH treatment also led to a significant decrease in the S2 (polymerized) fraction and an increase in the S1 (monomeric) pool of tubulin. Concomitant with these effects were marked decreases in cellular viability. DmPGE2 pretreatment abolished the disruption of microtubules, significantly increased the S2 fraction of tubulin, and increased cellular viability in cultures exposed to EtOH. Furthermore, pretreatment with colchicine, an inhibitor of microtubule assembly, prevented the cytoprotective action of dmPGE2. Taxol, a microtubule stabilizing agent, mimicked the effects of dmPGE2 by also enhancing microtubule integrity and increasing cellular viability in cells exposed to EtOH. These data indicate that organization and stabilization of microtubules may play an essential role in the mechanism of prostaglandin-induced protection.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ethanol injury protection by prostaglandin in human intestinal cell line and microtubule role)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 37 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:573288 HCAPLUS
DOCUMENT NUMBER: 127:243444
TITLE: Protective action of gastrin-17 against alcohol-induced gastric injury in the rat: role in mucosal defense
AUTHOR(S): Mercer, David W.; Cross, James M.; Smith, Gregory S.; Miller, Thomas A.
CORPORATE SOURCE: Department of Surgery, The University of Texas at Houston Medical School, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1997), 273(2, Pt. 1), G365-G373
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exogenous cholecystokinin (CCK) or exposure of the stomach to the mild irritant 25% ethanol can prevent gastric injury. Ingestion of ethanol also elicits the release of CCK as well as gastrin, which is structurally similar to CCK. This study was undertaken in conscious rats to examine the gastroprotective actions of gastrin and to assess the effect of CCK-gastrin receptor blockade on adaptive cytoprotection with ethanol as the mild irritant. I.v. (1-25 pmol/kg) administration of gastrin-17 dose dependently increased gastric mucosal blood flow (laser Doppler) and reduced gastric injury caused by 1 mL of orally administered acidified ethanol (150 mM HCl-50% ethanol). Similar gastroprotection was achieved with the gastrin secretagogue 5% peptone (1 mL orogastrically). The gastroprotective capabilities of gastrin-17 were attenuated by the type B CCK (gastrin) receptor antagonist L-365,260 (12.5-25 mg/kg i.p.) and by capsaicin desensitization (125 mg/kg s.c.). CCK octapeptide (5 nmol/kg i.v.)-induced protection was reversed by the type A CCK receptor antagonist MK-329 (1 mg/kg i.p.). Neither receptor antagonist, alone or in combination, reversed the protective effects of the mild irritant 25% ethanol (1 mL orogastrically). Thus, whereas gastrin may play a role in gastric mucosal defense, neither CCK nor gastrin appears to participate in the phenomenon of adaptive cytoprotection.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gastrin-17 protective action alc.-induced gastric injury in relation to mucosal defense)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

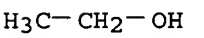
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 38 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:659701 HCAPLUS
DOCUMENT NUMBER: 125:318148
TITLE: Cholecystokinin-induced protection against gastric injury is independent of endogenous somatostatin
AUTHOR(S): Mercer, David W.; Klemm, Klaus; Cross, James M.; Smith, Gregory S.; Cashman, Mary; Miller, Thomas A.
CORPORATE SOURCE: Dep. Surgery, Univ. Texas Houston Med. Sch., Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1996), 271(4, Pt. 1), G692-G700
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cholecystokinin (CCK) prevents macroscopic injury to the stomach from luminal irritants by an unknown mechanism. The present study was undertaken in conscious rats to ascertain what role gastric mucosal blood flow, sensory neurons, and endogenous somatostatin play in CCK-induced gastric protection. S.c. administration of CCK (10-100 μg/kg) significantly reduced macroscopic injury to the acid-secreting portion of the stomach caused by 1 mL of orally administered acidified ethanol (150 mM HCl, 50% ethanol) and augmented gastric mucosal blood flow (fluorescent microspheres) in a dose-dependent fashion. However, although the protective response to CCK (100 μg/kg) was still present at 2 h, the blood flow response had returned to baseline by 45 min. Ablation of capsaicin-sensitive afferent neurons with capsaicin (125 mg/kg s.c.) did not negate CCK-induced protection. Pretreatment with exogenous somatostatin (1 pmol - 1 nmol/kg s.c.) failed to prevent the damaging effects of acidified ethanol to gastric mucosa. Immunoneutralization of endogenous somatostatin with somatostatin monoclonal antibody (2 mg i.p.) did not reverse the protective actions of CCK. Thus the data suggest that although CCK may prepare the gastric mucosa to withstand a damaging insult by augmenting gastric mucosal blood flow, its protective mechanism is independent of intact sensory neurons and endogenous somatostatin.

IT 64-17-5, Ethanol, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholecystokinin-induced protection against gastric injury is independent of endogenous somatostatin)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 39 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:438266 HCAPLUS
DOCUMENT NUMBER: 125:107619
TITLE: Gastric injury induced by ethanol and ischemia-reperfusion in the rat: Differing roles for lipid peroxidation and oxygen radicals
AUTHOR(S): Smith, Gregory S.; Mercer, David W.; Cross, James M.; Barreto, Jose C.; Miller, Thomas A.
CORPORATE SOURCE: Medical School, University Texas, Houston, TX, 63104, USA
SOURCE: Digestive Diseases and Sciences (1996),

41(6), 1157-1164
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

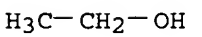
AB This study determined the role that oxygen-derived free radicals played in the production of gastric injury in rats challenged orally with concentrated ethanol or subjected to vascular compromise. In the ethanol study, rats were pretreated with a variety of free radical scavengers or enzyme inhibitors prior to exposing the stomach to 100% ethanol. At sacrifice, the degree of macroscopic damage to the glandular gastric mucosa was quantified. In sep. studies, the effects of ethanol on gastric mucosal levels of enaldehydes (malondialdehyde and 4-hydroxynonenal) were examined as an index of lipid peroxidn. Superoxide dismutase and catalase pretreatment were without benefit in reducing injury in the ethanol model, excluding potential contributory roles for the superoxide anion or hydrogen peroxide, resp. DMSO and desferoxamine were likewise without protective capabilities, eliminating a role for the hydroxyl radical. Allopurinol, a xanthine oxidase inhibitor, provided no protection under acute conditions, even though partial protection was noted when administered chronically. Further, enaldehyde levels were not increased over control levels in alc.-exposed mucosa, indicating no enhanced lipid peroxide formation. In contrast, in animals in which ischemia to the stomach was induced followed by reperfusion, marked gastric injury was observed in combination with enhanced enaldehyde levels. Prevention of enaldehyde formation by a 21-aminosteroid concomitantly prevented injury induced by ischemia-reperfusion. These findings support the conclusion that ischemia-reperfusion injury to the stomach is an oxygen-derived free radical process whereas ethanol-induced injury clearly involved some other process. Although allopurinal was partially protective against ethanol damage when administered chronically, observations in other models of injury suggest that this action is independent of its inhibitory effect on xanthine oxidase.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(gastric injury induced by ethanol and ischemia-reperfusion in relation to lipid peroxidn. and oxygen radicals)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 40 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:232400 HCAPLUS
DOCUMENT NUMBER: 124:314130
TITLE: Gastric injury and protection against alcohol and acid: influence of perturbations in glutathione metabolism
AUTHOR(S): Smith, Gregory S.; Tornwall, Michael S.; Barreto, Jose C.; Miller, Thomas A.
CORPORATE SOURCE: Medical School, University of Texas, Houston, TX, 77030, USA
SOURCE: Journal of Surgical Research (1996), 61(2), 395-403
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Academic

DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study assessed the role that inhibition of glutathione (GSH) synthesis and decreased GSH peroxidase (GPX) activity in the rat played in modulating gastric injury induced by ethanol and acid and its prevention by 16,16-dimethyl PGE2 (dmPGE2) and the mild irritant, 25% ethanol. Although numerous studies have proposed that GSH may be important in maintaining gastric mucosal defense, the exact role of this antioxidant in protecting the stomach from injury remains undefined. The present study addressed this consideration by blocking the synthesis of GSH and altering the major pathway by which it exhibits its antioxidant activity and determining the effect of these perturbations on gastric injury and protection. Four to six rats were used for each exptl. group. GSH synthesis was blocked by the potent and specific inhibitor L-buthionine sulfoximine (BSO), 2 or 6 mmole/kg i.p. The activity of the major form of GPX, which is selenium dependent and utilizes GSH as a substrate to detoxify hydrogen peroxide and other hydroperoxides, was inhibited by placing animals on a selenium-deficient diet for 6 wk. Gastric damage was induced by 100% ethanol, 50% ethanol in 150 mM HCl, and 0.75 M HCl. Prevention of such injury was accomplished with oral pretreatment using 25% ethanol or dmPGE2 (5 μg/kg). The damaging effects of 100% ethanol, 50% ethanol/150 mM HCl, or 0.75 M HCl were not adversely affected by BSO pretreatment even though GSH synthesis was inhibited by as much as 80%. Similarly, inhibition of GPX activity by 58% in adult rats and 98% in weanling rats failed to potentiate the damaging effect of 100% ethanol. Furthermore, with both perturbations in GSH metabolism, the protective action of dmPGE2 and 25% ethanol was maintained. Our results indicate that profound alterations in gastric GSH metabolism by themselves do not aggravate the injurious effects of ethanol or acid, nor do they prevent the protective action of a prostaglandin or mild irritant.
IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(glutathione metabolism role in gastric alc. and acid induced injury and prostaglandin protection)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 41 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:892389 HCAPLUS
DOCUMENT NUMBER: 124:48109
TITLE: The role of vagal innervation in adaptive cytoprotection
AUTHOR(S): Miller, Thomas A.; Smith, Gregory S.; Tornwall, Michael S.; Lopez, Rafael A.; Henagan, Julia M.; Schmidt, Karmen L.
CORPORATE SOURCE: Dep. of Surgery, The Univ. of Texas Medical School, Houston, TX, 77030, USA
SOURCE: Hans Selye Symposia on Neuroendocrinology and Stress (1995), 2(Neuroendocrinology of Gastrointestinal Ulceration), 191-200
CODEN: HSNSFN
PUBLISHER: Plenum
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A previous study showed that ethanol-induced injury in the rat stomach could be enhanced with vagotomy. The authors studied what role capsaicin-sensitive fibers may play in the mediation of these vagotomy effects. The studies indicated that functional ablation of capsaicin-sensitive fibers does not reverse adaptive cytoprotection. The ability of both 25% ethanol and low dose capsaicin to prevent injury induced by 100% ethanol suggests that the two agents mediate their protective effects through different mechanisms.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effect of vagotomy on ethanol-induced stomach injury in relation to capsaicin-sensitive vagal fibers)

RN 64-17-5 HCAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 42 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:523702 HCAPLUS

DOCUMENT NUMBER: 122:282708

TITLE: Cholecystokinin is a potent protective agent against alcohol-induced gastric injury in the rat: Role of endogenous prostaglandins

AUTHOR(S): Mercer, David W.; Cross, James M.; Barreto, Jose C.; Strobel, Nathaniel H.P.; Russell, Diane H.; Miller, Thomas A.

CORPORATE SOURCE: Medical School, University of Texas, Houston, TX, 77030, USA

SOURCE: Digestive Diseases and Sciences (1995), 40(3), 651-60
CODEN: DDSCDJ; ISSN: 0163-2116

DOCUMENT TYPE: Journal

LANGUAGE: English

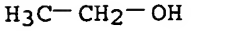
AB This study was undertaken to ascertain whether cholecystokinin could prevent the gastric mucosal injury induced by acidified ethanol and what role prostaglandins, and type A and type B cholecystokinin receptors might play in this process. Conscious, fasted rats were given s.c. saline or cholecystokinin octapeptide (10-100 μg/kg) 30 min before a 1-mL oral gastric bolus of acidified ethanol (150 mM HCl/50% ethanol). Five minutes later, rats were sacrificed and the total area of macroscopic injury quantitated (square millimeters). In addnl. expts. using a similar protocol, 1 mL of either the cyclooxygenase inhibitor, indomethacin (5 mg/kg), a type A cholecystokinin receptor antagonist, L-364,718 (0.01-1 mg/kg), or the type B cholecystokinin receptor antagonist, L-365,260 (12.5-25 mg/kg) was given i.p. 30 min prior to pretreatment with cholecystokinin octapeptide. Cholecystokinin octapeptide dose-dependently prevented mucosal injury from acidified ethanol (corroborated by histol.). The protective effect of cholecystokinin octapeptide was completely negated by L-364,718 and partially reversed by indomethacin, while L-365,260 had no discernible effect in this process. In a further study, cholecystokinin was unable to prevent the damaging effects of aspirin and the inhibition of endogenous prostaglandins. Thus, it appears that cholecystokinin is able to maintain mucosal integrity in the face of a damaging insult by activation of type A cholecystokinin receptors, an effect mediated, at least in part, through the release of endogenous prostaglandins.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cholecystokinin protection against alc.-induced gastric injury mediation by endogenous prostaglandins)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

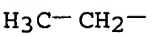
H_3C-CH_2-OH

L38 ANSWER 43 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:447241 HCAPLUS
DOCUMENT NUMBER: 122:207543
TITLE: Gastric mucosal high-energy phosphate metabolism. Influence of ethanol and PGE2
AUTHOR(S): Victor, Brant E.; Taegtmeyer, Heinrich; Miller, Thomas A.
CORPORATE SOURCE: Departments Surgery and Internal Medicine/Cardiology, University Texas Medical School, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1995), 40(1), 120-7
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated potential alterations in gastric mucosal energy metabolism following exposure to the damaging agent 50% ethanol (50% EtOH) alone and after pretreatment with either 16,16-dimethyl (dmPGE2) or the mild irritant 25% ethanol (25% EtOH). Fasted rats (n = 12-26/group) were orally given 1 mL of normal saline (NS), dmPGE2 in a dose of 5 μg/kg, or 25% EtOH. Fifteen minutes later, they randomly received 1 mL of NS or 50% EtOH. After 5 min, rats were anesthetized and their stomachs rapidly excised, frozen in liquid nitrogen, and lyophilized. Once dried, the surface area (in square millimeters) of mucosal lesions was quantitated. Mucosa was then scraped off the underlying muscularis. Tissue metabolites (ATP, ADP, AMP, lactate, pyruvate, glucose, and glucose-6-phosphate) were measured in deproteinized, neutralized samples by enzymic methods. In conjunction with the development of mucosal lesions involving an average of 45 mm2, ATP was significantly ($P < 0.05$) lower and AMP significantly higher in 50% EtOH-treated animals (indicating dephosphorylation) when compared with NS controls. Although both 25% EtOH and dmPGE2 prevented these lesions, only 25% EtOH prevented the ATP and AMP alterations. Fifty percent EtOH also significantly increased the tissue content of glucose and lactate over control values while glucose-6-phosphate was significantly decreased. With both protective agents pyruvate levels were significantly reduced, while glucose and lactate levels were not affected. In contrast to dmPGE2, the mild irritant (25% EtOH) significantly increased glucose-6-phosphate levels over control. These results indicate that the protective action of 25% EtOH is associated with prevention of the adverse effects of 50% EtOH on oxidative phosphorylation, whereas that of dmPGE2 involves a different mechanism.
IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ethanol effect on gastric mucosal high-energy phosphate metabolism)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 44 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:295702 HCAPLUS
DOCUMENT NUMBER: 120:295702
TITLE: Adverse effects of vagotomy on ethanol -induced gastric injury in the rat: absence of a role for glutathione redox cycle
AUTHOR(S): Tornwall, Michael S.; Smith, Gregory S.; Barreto, Jose C.; Lopez, Rafael A.; Henagan, Julia M.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1993), 38(12), 2294-8
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Truncal vagotomy is known to aggravate the damaging effects of alc .-induced gastric injury and prevent the occurrence of adaptive cytoprotection against such injury by a mild irritant. This study was undertaken to determine whether aberrations in glutathione (GSH) metabolism were responsible for these vagotomy-induced effects. Fasted rats (6-8/group) were subjected to truncal vagotomy and pyloroplasty or sham vagotomy and pyloroplasty. One week later they were given 2 mL of oral saline or the mild irritant, 25% ethanol (EtOH). Thirty minutes following such treatment, animals were either sacrificed or orally received 2 mL of 100% EtOH and then were sacrificed 5 min later. At sacrifice, in each exptl. group, stomachs were removed and either evaluated macroscopically for the degree of injury involving the glandular gastric epithelium or samples of the mucosa were prepared for measurement of total GSH levels or GSH peroxidase (GPX) and GSH reductase (GRT) activity. In nonvagotomized animals, saline treatment prior to 100% EtOH exposure resulted in injury to the glandular epithelium involving approx. 18%. Treatment with 25% EtOH prior to 100% EtOH exposure virtually abolished this injury. In vagotomized animals, 100% EtOH elicited almost three times the amount of injury observed in the nonvagotomized state and the protective effect of 25% EtOH pretreatment was prevented. Effects of the various treatment modalities on GPX and GRT activity were not significantly different from control values. When mucosal GSH results were plotted against the presence or absence of gastric injury among the various groups studied, no significant correlation was apparent. Thus, aberrations in glutathione metabolism do not explain the absence of adaptive cytoprotection following vagotomy or the exacerbation of alc.-induced damage under conditions of vagal denervation.
IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(gastric injury from, vagotomy exacerbation of, aberrations of glutathione metabolism role in)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 45 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:619288 HCAPLUS
DOCUMENT NUMBER: 119:219288
TITLE: Gastric damage caused by acidified ethanol: Role of molecular hydrochloric acid
AUTHOR(S): Barreto, Jose C.; Smith, Gregory S.; Russell, Diane H.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1993), 265(1, Pt. 1), G133-G137
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was undertaken to test the hypothesis that an increase in the concentration of mol. HCl in ethanolic solns. is at least partly responsible for the severity of damage seen with acidified ethanol. To accomplish this goal, the authors studied the synergistic relationship of HCl and ethanol by holding ethanol constant at 50% (volume/volume) and varying the acid concentration In another experiment, acid concentration was held constant at 150 mM HCl, and the percentage of ethanol was varied. The authors' hypothesis was also tested by substituting sulfate for chloride to form H2SO4, a nonpermeant mol. acid. The substitution of sulfate for chloride greatly reduced gastric damage, supporting the hypothesis that diffusion of mol. HCl is contributing to the damage by acidifying cells. In all cases, acidified ethanol solns. using HCl were more damaging than the individual components alone, and the severity of the damage caused by 50% ethanol was dependent on the concentration of HCl. Thus, the severity of acidified ethanol damage is dependent on cellular acidification caused by diffusion of mol. HCl.
IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(stomach damage from acidified, mol. hydrochloric acid role in)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

L38 ANSWER 46 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:577843 HCAPLUS
DOCUMENT NUMBER: 119:177843
TITLE: Crustacean cardioactive peptide in the sphinx moth, Manduca sexta
AUTHOR(S): Lehman, H. K.; Murgiuc, C. M.; Miller, T. A. ; Lee, T. D.; Hildebrand, J. G.
CORPORATE SOURCE: ARL Div. Neurobiol., Univ. Arizona, Tucson, AZ, 85721, USA
SOURCE: Peptides (New York, NY, United States) (1993), 14(4), 735-41
CODEN: PPTDD5; ISSN: 0196-9781

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The isolation, identification, and actions of crustacean cardioactive peptide (CCAP) have been examined in the sphinx moth M. sexta. A sensitive and specific ELISA was used to quantify CCAP-like immunoreactivity in the nervous system. The CCAP-like immunoreactivity from the abdominal CNS was then purified, and its sequence was ascertained by amino acid anal., mass spectral anal., and HPLC. These studies showed that the nervous system of M. sexta contains a peptide with the sequence Pro -Phe-Cys-Asn-Ala-Phe-Thr-Gly-Cys-NH2, identical to CCAP originally isolated and sequenced from the shore crab Carcinus maenas. The actions of CCAP on the isolated heart of M. sexta and the extensor-tibia muscle of Schistocerca ameoicana were tested. Crustacean cardioactive peptide had excitatory actions on both prepns.: a dose-dependent increase in the rate of contractions was observed on the heart, and an increase in the rate of the myogenic rhythm was observed in the leg muscle. Moreover, purified and synthetic CCAP had identical effects on the isolated heart. The authors conclude that CCAP occurs in M. sexta and exerts potent neurotransmitter or neurohormonal actions on a variety of muscles.

L38 ANSWER 47 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:400686 HCAPLUS
DOCUMENT NUMBER: 119:686
TITLE: Protective action of oral N-acetylcysteine against gastric injury: Role of hypertonic sodium
AUTHOR(S): Barreto, Jose C.; Smith, Gregory S.; Tornwall, Michael S.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1993), 264(3, Pt. 1), G422-G426
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-Acetylcysteine (NAC), when administered orally as a 20% solution, is a potent protective agent against gastric injury in the rat stomach induced by absolute ethanol. The present study was undertaken to define the means by which this protection is mediated. The notion that NAC acts as a glutathione precursor was excluded when N-acetylserine (NAS) was noted to be equally protective against alc. injury. The NAS mol. contains a hydroxyl moiety at the site where NAC contains a sulfhydryl. To orally administer 20% NAC at a neutral pH, NaOH is added to the free acid form to keep NAC in solution We determined by titration that a sodium concentration of 1.2 M results. Thus it became apparent that the protective effect of NAC might be mediated through the sodium employed to titrate NAC. Accordingly, we examined various sodium salts and assessed their relative protective effects against alc. injury. Both sodium acetate and sodium chloride in 1 M solns. were found to be equally effective in preventing alc. injury with the same efficiency as 1 M sodium solns. of NAC and NAS, excluding the acetate portion of NAC and NAS as being of primary importance for protection to occur. Further study, using different concns. of sodium chloride (i.e., 150-1,000 mM) revealed that the 1 M solution was most optimal in preventing alc. injury. One molar sodium by itself and when administered as part of the NAC solution also prevented gastric injury by concentrated acid and base. Finally, dilution of the damaging agent from potential pooling of fluid from the gastric mucosa was found not to be responsible for the protective action of hypertonic sodium, nor were endogenous prostaglandins since indomethacin did not block this action. We conclude that the protective action of NAC when

given orally as a 20% solution appears to be a function of its high sodium content through a mechanism yet to be defined.

L38 ANSWER 48 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:17823 HCAPLUS
DOCUMENT NUMBER: 118:17823
TITLE: Gender differences in ethanol oxidation and injury in the rat stomach
AUTHOR(S): Lee, Lorna; Schmidt, Karmen L.; Tornwall, Michael S.; Henagan, Julia M.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Alcohol (New York, NY, United States) (1992), 9(5), 421-5
CODEN: ALCOEX; ISSN: 0741-8329
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was undertaken to determine if gender influences the magnitude of ethanol-induced injury in rat gastric mucosa and whether any differences can be linked to altered levels of alc. dehydrogenase (ADH) activity. Since prostaglandins (PGs) markedly attenuate the severity of gastric injury induced by ethanol in the rat stomach, a further goal of this study was to determine whether the efficiency of PG's protective action was in any way influenced by gender. Accordingly, both male and female were pretreated s.c. with 16,16-dimethyl PGE2 (10 μg/kg) or saline 30 min prior to administering an oral dose of 50% ethanol in saline or saline alone. They were then sacrificed 5 min later. In a portion of animals, samples of mucosa from the glandular stomach were obtained and kinetic activity of ADH determined In another portion of animals, gastric tissue samples from the glandular mucosa were examined by light microscopy and the magnitude of mucosal injury quantified. Alc.-treated females showed significantly less superficial and more deep mucosal injury than male counterparts. Further, ADH kinetic activity in female rats was significantly less than that observed in male counterparts of similar weight Despite these differences in ADH activity, and the magnitude of mucosal injury, the efficiency of protection by PG was equivalent in both sexes and involved primarily the deep epithelium. The results of this study indicate that ethanol damage to the gastric mucosa in female rats is more severe than that in corresponding males, and may be linked to the lower ADH kinetic activity present in female gastric mucosa. Despite these differences in ethanol oxidation and gastric injury, PG's protective action was equally efficacious in both sexes, indicating that gender differences in ADH activity were of no importance in mediating this protection.
IT 9031-72-5, Alcohol dehydrogenase
RL: BIOL (Biological study)
(of stomach, during ethanol-induced stomach injury, gender difference in)
RN 9031-72-5 HCAPLUS
CN Dehydrogenase, alcohol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to stomach, gender difference in)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 49 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:626074 HCAPLUS
DOCUMENT NUMBER: 117:226074
TITLE: Protective effect of dimethylthiourea against mucosal injury in rat stomach. Implications for hydroxyl radical mechanism
AUTHOR(S): Smith, Gregory S.; Barreto, Jose C.; Schmidt, Karmen L.; Tornwall, Michael S.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1992), 37(9), 1345-55
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was undertaken to determine whether dimethylthiourea (DMTU), a hydroxyl radical scavenger, could prevent gastric injury in the rat stomach induced by various noxious agents. Fasted rats (N = 6-8/group) were given a 1-mL oral bolus of saline or DMTU over the dose range 10-500 mg/kg. After 30 min, animals received 1 mL of 100% ethanol orally and were sacrificed 5 min later. At sacrifice, stomachs were harvested and the degree of macroscopic damage was assessed by planimetry. In selected animals, specimens of gastric mucosa were also processed for histol. Saline pretreatment prior to ethanol exposure resulted in 22.5% injury to the glandular epithelium when assessed macroscopically. DMTU pretreatment prevented such injury in a dose-related fashion with only 2% of the mucosa showing injury with a 500 mg/kg dose ($P < 0.01$ vs control). Although the superficial injury involving surface mucous cells induced by ethanol was not altered by DMTU, the deep damage to gastric glands was almost completely prevented. Other expts. in which DMTU was given i.p. demonstrated similar protective effects against ethanol injury. Addnl. studies showed that indomethacin did not prevent the protective effects of oral or i.p. DMTU, excluding a role for endogenous prostaglandins, and that DMTU was equally protective when administered within minutes or as long as 2 h prior to ethanol exposure. Furthermore, DMTU was also shown to be protective against gastric injury induced by concentrated acid or base. In in vitro studies in which hydroxyl radicals were actually generated, DMTU was noted to scavenge the hydroxyl radical in a dose-related fashion. The ability of DMTU to prevent gastric injury by three different damaging agents suggests that the hydroxyl radical may play a major role in the pathogenesis of such injury and that DMTU mediated its protective action by scavenging this radical species.

L38 ANSWER 50 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:162794 HCAPLUS
DOCUMENT NUMBER: 116:162794
TITLE: Interface formation and growth of indium antimonide on silicon (100)
AUTHOR(S): Franklin, G. E.; Rich, D. H.; Hong, Hawoong; Miller, T.; Chiang, T. C.
CORPORATE SOURCE: Dep. Phys., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Physical Review B: Condensed Matter and Materials Physics (1992), 45(7), 3426-34
CODEN: PRBMDO; ISSN: 0163-1829
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High-energy electron diffraction, Auger spectroscopy, photoemission, and x-ray diffraction were used to study the

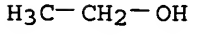
interface and subsequent growth of InSb on vicinal (4° off) and on-axis Si(100). During the initial stages of mol.-beam epitaxy at 410°, the In, Sb, and Si core levels were examined as a function of In and Sb coverage and deposition order. Based on these results, a model for interface formation is developed. Thicker coverage results of coevaporated InSb are discussed in light of the interfacial analyses.

L38 ANSWER 51 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:100947 HCAPLUS
DOCUMENT NUMBER: 116:100947
TITLE: Protection against ethanol injury in the canine stomach: role of mucosal glutathione
AUTHOR(S): Victor, Brant E.; Schmidt, Karmen L.; Smith, Gregory S.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1991), 261(6, Pt. 1), G966-G973
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study determined the role that mucosal GSH levels play in mediating the protective effects of a prostaglandin and a mild irritant against alc.-induced gastric injury. An in vivo canine chambered stomach preparation was used in which the exteriorized mucosa was partitioned into two equal halves, one serving as control. Animals (5-8/group) received a s.c. injection of either normal saline (NS) or the GSH depletor N-ethylmaleimide (NEM; 50 mg/kg) and then were assigned to one of a variety of groups based on the perfusate used to bath the exptl. side of the chamber; NS bathed the control mucosa. At completion of the studies, mucosa from each side of the chamber was assayed for total GSH (μmol/g wet weight) and evaluated for microscopic damage. Both 16,16-dimethyl prostaglandin E2 (PGE2) (1 μg/mL) and the mild irritant 8% ethanol, when topically applied to the gastric epithelium, increased mucosal GSH levels by .apprx.20% compared with control values, and elicited no deleterious effects to the mucosa. Treatment of animals with NEM prevented these GSH effects by PGE2 and 8% ethanol without damaging the mucosa. Application of 40% ethanol to the mucosa markedly reduced levels of GSH and caused significant injury to the mucosal surface, much of it extending to the level of the gastric glands. When mucosa was pretreated with PGE2 or 8% ethanol before 40% ethanol exposure, deep gastric gland injury was virtually abolished. In animals receiving NEM, the protective effects of these agents against injury by 40% ethanol were prevented. Perturbations in tissue levels of GSH under these various exptl. conditions failed to correlate histol. with the status of gastric mucosal integrity. The authors conclude that while PGE2 and 8% ethanol enhanced GSH levels in gastric mucosa, possibly by inducing synthesis of GSH, this circumstance did not account for the ability of these agents to enable the mucosa to resist the deep damage elicited by 40% ethanol.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to stomach, glutathione in relation to)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 52 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:508380 HCAPLUS
DOCUMENT NUMBER: 115:108380
TITLE: Colloidal gold localization of type IV collagen in the extracellular matrix of rat gastric mucosa: influence of alcohol and prostaglandin
AUTHOR(S): Rightor, Kathryn S.; Mitchell, Philip A.; Miller, Thomas A.; Schmidt, Karmen L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Anatomical Record (1991), 230(2), 235-42
CODEN: ANREAK; ISSN: 0003-276X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of acute alc. exposure on the gastric mucosal basal lamina, and its major structural protein type IV collagen, was assessed by transmission electron microscopy (TEM) and immunogold (IG) labeling of this collagenous material. Fasted rats orally received either 50% or 100% ethanol. Five or 60 min later animals were sacrificed and mucosal samples were obtained from the glandular epithelium for TEM or IG localization of type IV collagen. For IG studies, the number of gold particles/area lamina densa was quantified in interfoveolar, pit, and gland regions as an index of the mol. integrity of type IV collagen. Both ethanol concns. induced epithelial exfoliation with pleating of the denuded lamina densa. Absolute ethanol, and to a lesser extent 50% ethanol, caused frequent rupture of a thickened, precipitated lamina densa. Immunolabeling of type IV collagen varied with the exptl. protocol. In control tissues exposed to oral saline, binding was greatest in the interfoveolar zone. Low binding occurred with 100% ethanol in all regions when compared with controls, but 50% ethanol evoked significantly higher binding in interfoveolar regions, in a similar fashion to controls. In addnl. studies in which 16.16 di-Me prostaglandin E2 (PGE2) (10 μg/kg) was injected s.c. prior to oral ethanol exposure, PGE2 pretreatment prevented the large decrease in IG binding induced by absolute ethanol, but the level still remained significantly less than with corresponding controls. In contrast, pretreatment with PGE2 prior to 50% ethanol exposure restored type IV collagen immunolabeling to control levels. Thus, ethanol induces a concentration-dependent lowering of IG binding to type IV collagen which also effects its reversibility by PGE2.
IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(type IV collagen localization in gastric mucosa by immunogold response to PGE2 and)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 53 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:505800 HCAPLUS
DOCUMENT NUMBER: 115:105800
TITLE: N-Acetylcysteine: protective agent or promoter of gastric damage?
AUTHOR(S): Lopez, R. A.; Tornwall, M. S.; Henagan, J. M.; Smith, G. S.; Miller, T. A.
CORPORATE SOURCE: Sch. Med., Univ. Puerto Rico, San Juan, 00926, P. R.

SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1991), 197(3), 273-8
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-acetylcysteine (NAC), when given orally, has been shown to prevent gastric damage induced by ethanol, but when administered i.p., it appears to potentiate such damage. In an effort to resolve these seemingly discordant findings, fasted rats (six per group) received 1 mL of saline or 20% NAC orally or i.p. Two hours or 15 min later, they received 1 mL of 100% ethanol orally. At sacrifice 5 min later, rats receiving oral pretreatment with 20% NAC at both 15 and 120 min prior to ethanol exposure had significantly less gastric injury when compared with saline controls. In contrast, promotion of ethanol damage was noted when NAC was given i.p.; the injury was more pronounced when NAC was administered 15 min prior to exposing the mucosa to 100% ethanol. In all animals receiving i.p. NAC, large amts. of peritoneal fluid (4-6 mL/rat) were recovered at the time of sacrifice, most of which occurred within 15 min of NAC administration; these more pronounced peritoneal effects at 15 min after NAC correlated with the more severe injury from ethanol at this time period compared to that observed 120 min after i.p. NAC. Saline controls had no peritoneal fluid. Mucosal glutathione (GSH) levels generally paralleled these results in that a significant decrease in tissue GSH occurred at 15 min following i.p. NAC when compared with controls; at 120 min after i.p. NAC, GSH levels were similar to control values. Addnl. expts. demonstrated that within 15 min following NAC administration, systemic blood pressure dropped by approx. 20% and basically remained unchanged over the next 2 h; i.p. saline had no sustained adverse effects on blood pressure. It was concluded that the inability of NAC to prevent ethanol injury when given i.p. in contrast to when administered orally is related to the drop in blood pressure secondary to NAC's peritoneal irritant effects, which presumably altered gastric mucosal blood flow, thus inhibiting its ability to prevent ethanol damage under these conditions. Furthermore, the decreased levels in mucosal GSH following the hypotension induced by i.p. NAC suggest that perturbations in GSH metabolism may also have contributed to the decreased resistance to ethanol injury.

IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(stomach damage from, acetylcysteine effect on, after i.p. and oral administration)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 54 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:503735 HCAPLUS
DOCUMENT NUMBER: 115:103735
TITLE: Crystallization of bismuth strontium calcium copper oxide (Bi2Sr2CaCu2Ox) superconducting filaments produced by gas-jet fiberization
AUTHOR(S): Jacobs, K. R.; Miller, T. A.; Finnemore, D. K.; Goldman, A. I.; Lebeau, S. E.; Righi, J.
CORPORATE SOURCE: Dep. Phys., Iowa State Univ., Ames, IA, 50011, USA
SOURCE: IEEE Transactions on Magnetics (1991), 27(2, Pt. 2), 917-19

CODEN: IEMGAQ; ISSN: 0018-9464
DOCUMENT TYPE: Journal
LANGUAGE: English
AB X-ray diffraction and differential thermal anal. techniques have been used to investigate the recrystn. products obtained from various heat treatments of glassy Bi2Sr2CaCu2Ox filaments produced by the gas-jet fiberization process. In both Pb-doped and Pb-free samples, the 85K superconducting phase appears after the formation of a disordered Bi2Sr2CuOx-like intermediate phase at lower temperature The c-lattice parameter of this phase is substantially smaller than the published values for Bi2Sr2CuOx and increases as the published values for Bi2Sr2CUOx and increases as the temperature of the heat treatment increases. After heat treatment at 600°, a Pb-rich second phase is found together with the 2201-like intermediate phase in the Pb-doped material.

L38 ANSWER 55 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:242605 HCAPLUS
DOCUMENT NUMBER: 114:242605
TITLE: Effects of alcohol on lectin binding affinity in rat gastric mucosa
AUTHOR(S): Mitchell, Philip A.; Miller, Thomas A.; Schmidt, Karmen L.
CORPORATE SOURCE: Health Sci. Cent., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1990), 35(7), 865-72
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluoresceinated lectins were employed to qual. evaluate cell surface carbohydrates, with and without ethanol exposure, in rat stomach mucosas. Rats received 1 mL of saline, or 50% or 100% ethanol orally. After 30 min, tissue samples of the glandular stomach were retrieved, cryosectioned, and incubated with one of a panel of lectins. Another set of sections was preincubated with neuraminidase to remove sialic acid residues. Qual. evaluation of lectin binding showed that although several different sites stained, Con A was the only lectin to stain the extracellular matrix, and soybean agglutinin the only lectin to stain chief cells. Neuraminidase preincubation enhanced lectin binding to both stained and previously unstained sites. Ethanol, both 50% and 100%, produced changes in both neuraminidase-treated and untreated tissues, increasing the specific binding of Con A, Ulex europaeus agglutinin I, and wheat germ agglutinin, while decreasing Helix pomatia agglutinin and soybean agglutinin. These results suggest that ethanol can, through unknown mechanisms, alter carbohydrate binding affinity.
IT 64-17-5, Ethanol, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(lectin binding in gastric mucosa response to)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 56 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:199532 HCAPLUS

DOCUMENT NUMBER: 114:199532
TITLE: Neuroexcitatory drug receptors in mammals and invertebrates
AUTHOR(S): Miller, T. A.; Olsen, R. W.
CORPORATE SOURCE: Univ. California, Los Angeles, CA, USA
SOURCE: Report (1990), ARO-24118.3-LS; Order No. AD-A220255, 9 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1990, 90(15), Abstr. No. 039,157
DOCUMENT TYPE: Report
LANGUAGE: English

AB Previous work by the principal investigators and others has shown that the major type of synaptic receptor for the major inhibitory neurotransmitter, the GABA-A receptor/chloride channel complex, is the target of numerous drugs and toxins. The GABA-A receptor function is directly potentiated by several categories of central nervous system depressants including benzodiazepines, barbiturates, steroid anesthetics, avermectin pesticides, and possibly ethanol. GABA-A receptor function is directly blocked by the GABA antagonist bicuculline, benzodiazepine inverse agonists, convulsant barbiturates, and a series of cyclic convulsant mols. like picrotoxin. These neuroexcitatory GABA blockers include pentylenetetrazol, chlorinated hydrocarbon insecticides like dieldrin and lindane, and the synthetic cage convulsants of Casida, such as tert-Bu bicyclophosphorothionate (TBPS), one of the most toxic substances to mammals ever encountered. It was demonstrated that these convulsant drugs acted potently on GABA-A receptors in mammals and invertebrates, using a combination of electrophysiol. and biochem. Structural and pharmacol. comparisons of the different subtypes of GABA-A receptors in various species and in various regions of human brain are underway. This will help to define the specificity of the neurotransmitter and drug binding sites in the various receptors and should lead to the development of new useful drugs.

L38 ANSWER 57 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:158962 HCAPLUS
DOCUMENT NUMBER: 114:158962
TITLE: Adaptive cytoprotection against alcohol injury in the rat stomach is not due to increased prostanoid synthesis
AUTHOR(S): Smith, G. S.; Myers, S. I.; Bartula, L. L.; Miller, T. A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Prostaglandins (1991), 41(3), 207-23
CODEN: PRGLBA; ISSN: 0090-6980
DOCUMENT TYPE: Journal
LANGUAGE: English

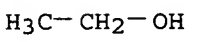
AB This study evaluated the effects of 25% ethanol, a mild irritant, on endogenous prostanoid synthesis in the rat stomach before and after exposure to oral 100% ethanol. Rats received water or 25% ethanol orally. After 15 min, a portion of each group was sacrificed and the remaining animals treated with 100% ethanol prior to sacrifice one minute later. Microsomal membrane fractions were prepared from the glandular gastric mucosa in all groups and incubated with [14C]arachidonic acid in the presence of cofactors. Endogenous mucosal prostanoid synthesis was analyzed by radiochromatog. and the results correlated with the presence or absence of gastric injury macroscopically. Prostanoids measured included PGI2, PGF2α, PGE2, PGD2, PGA2, and thromboxane A2. Addnl. expts. were performed in like manner to those just described with the exception that indomethacin (5 mg/kg i.p.) pretreatment was rendered. Stomachs exposed to water or 25% ethanol alone

demonstrated a modest and equivalent level of synthesis of all prostanoids measured. Exposure to 100% ethanol (with and without mild irritant pretreatment) significantly increased prostanoid synthesis (especially PGI2, PGF2α, and PGE2) compared with stomachs exposed to water or 25% ethanol alone; only mild irritant-treated mucosa was protected from injury by 100% ethanol. Indomethacin pretreatment reversed the increased prostanoid synthesis in mucosa exposed to 100% ethanol, with or without mild irritant pretreatment, and partially reversed the protective effect of 25% ethanol. Other expts. using tissue slices in which perturbations in mucosal levels of prostanoids were measured by RIA under identical exptl. conditions exhibited similar results. These data dispute the notion that adaptive cytoprotection is mediated by increased endogenous prostanoid synthesis. The partial reversal of this process by indomethacin was most likely secondary to some other action of this agent, such as a reduction in gastric blood flow, rather than direct effects on prostanoid synthesis.

IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(cryoprotection against injury from, in stomach)

RN 64-17-5 HCAPLUS

CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 58 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:7982 HCAPLUS

DOCUMENT NUMBER: 112:7982

TITLE: Poly(3-hydroxyoxetane) - an analog of poly(vinyl alcohol): synthesis, characterization, and properties

AUTHOR(S): Vandenberg, E. J.; Mullis, J. C.; Juvet, R. S., Jr.; Miller, T.; Nieman, R. A.

CORPORATE SOURCE: Dep. Chem., Arizona State Univ., Tempe, AZ, 85287-1604, USA

SOURCE: Journal of Polymer Science, Part A: Polymer Chemistry (1989), 27(9), 3113-49
CODEN: JPACEC; ISSN: 0887-624X

DOCUMENT TYPE: Journal

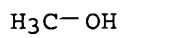
LANGUAGE: English

AB The spontaneous polymer formed from 3-hydroxyoxetane (I) is linear, low-mol.-weight, water-soluble, atactic poly(3-hydroxyoxetane) (II) of high crystallinity with -OCH2CH(OH)CH2OH end units. The highly crystalline nature of II may be related to the crystalline nature of atactic poly(vinyl alc.) since I can be considered a copolymer of vinyl alc . and HCHO. Spontaneous II apparently is formed in a cationic polymerization by the carboxylic acids produced by the air oxidation of I on standing at room temperature for several months. The polymerization can be duplicated by the addition of 2% hydroxyacetic acid to I. The rate of this unusual cationic polymerization increases greatly with acid strength, e.g., trifluoromethanesulfonic acid reacts explosively with pure I. A mechanism is proposed for this cationic polymerization High-mol.-weight, water-soluble, linear, atactic, and highly crystalline II (m.p. = 155°) was made by polymerizing the trimethylsilyl ether of I with the iso-Bu3Al-0.7H2O cationic catalyst followed by hydrolysis. Two 1H NMR methods for measuring the tacticity of II were developed based on

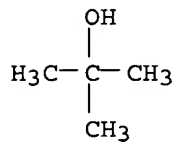
finding two different types of methylene units at 400 MHz with the methine protons decoupled. Also, an 1H-NMR method was developed for measuring branching in II. High-mol.-weight, linear II with enhanced isotacticity (80%) was obtained in low yield as a water-insol. fraction with Tm = 223°. The low-mol.-weight II prepared previously by the base-catalyzed, rearrangement polymerization of glycidol is highly branched.

IT 67-56-1, Methanol, uses and miscellaneous
75-65-0, tert-Butanol, uses and miscellaneous
RL: CAT (Catalyst use); USES (Uses)
(catalysts containing, for polymerization of (trimethylsilyloxy)oxetane)

RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



RN 75-65-0 HCAPLUS
CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)



L38 ANSWER 59 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:167955 HCAPLUS
DOCUMENT NUMBER: 110:167955
TITLE: Microscopic correlates of adaptive cytoprotection in an ethanol injury model
AUTHOR(S): Schmidt, Karmen L.; Smith, Gregory S.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Histology and Histopathology (1989), 4(1), 105-15
CODEN: HIHIES; ISSN: 0213-3911
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study histol. investigated the efficacy of pretreating rat gastric mucosa with the mild irritants, 10% and 25% EtOH, against the known damaging effects of 100% EtOH. Fasted rats received 1 mL of either water, 10% EtOH, or 25% EtOH by orogastric intubation. Fifteen minutes later, a portion of these animals was sacrificed and tissue samples of the oxyntic region of the stomach were excised and processed for quant. histol. anal. Remaining animals received a 1 mL oral bolus of the necrotizing agent, 100% EtOH. Five minutes later, these animals were sacrificed and tissues were prepared in a like manner. In a sep. series of expts., the aforementioned protocols were repeated, except that all animals received the prostaglandin synthetase inhibitor, indomethacin (5.0 mg/kg, i.p.) 30 min before administration of the mild irritant. Microscopically, the administration of water or 10% EtOH alone caused a small and comparable amount of superficial injury to the gastric mucosa. Moreover, both substances failed to induce protection in stomachs subsequently exposed to 100% EtOH. Indomethacin pretreatment did not significantly alter any of these findings. In marked contrast, 25% EtOH alone elicited a substantial degree of superficial damage to the gastric

mucosa. Nevertheless it significantly reduced the depth of injury in animals subsequently challenged by 100% EtOH. Indomethacin failed to aggravate the effects of 25% EtOH alone, but partially inhibited the protective effect of this mild irritant against 100% EtOH induced damage. Evidently, adaptive cytoprotection is a real phenomenon that can be demonstrated microscopically. Such protection is limited primarily to the deep mucosal layers (i.e. gastric glands), appears in part to be prostaglandin-mediated, and seems to require the generation of moderate surface cell damage (as occurred with 25% EtOH, but not 10% EtOH) to induce its initiation.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to stomach mucosa, adaptation response in relation to)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

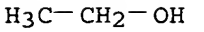
H_3C-CH_2-OH

L38 ANSWER 60 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:523080 HCAPLUS
DOCUMENT NUMBER: 109:123080
TITLE: Morphological characteristics of prostaglandin cytoprotection
AUTHOR(S): Schmidt, Karmen L.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77225, USA
SOURCE: Toxicologic Pathology (1988), 16(2), 223-36
CODEN: TOPADD; ISSN: 0192-6233
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To determine whether prostaglandins possess cytoprotective properties and if such effects are dependent on the dose and the route of prostaglandin administration, studies were performed using 16,16-dimethylprostaglandin E2 (PGE2) and the known gastric damaging agent ethanol. Fasted rats received either oral or s.c. PGE2 in doses of 10 or 20 μg/kg or equal vols. of saline. Thirty minutes later, animals were given a 1-mL oral bolus of 50% or 100% ethanol or an equal volume of saline. At 5 min-24 h following ethanol, animals were sacrificed, and tissues from the glandular portion of the stomach were removed for histol. quantification of injury. At 5 min following ethanol, PGE2 reduced the depth of injury, but had no protective effects against surface cell damage when compared with control animals. By 24 h after ethanol, most of the PGE2-treated mucosa was repaired. Oral administration of 10 μg PGE2/kg was more cytoprotective at 5 min after ethanol than when administered by s.c. injection. This relation was not true for the 20 μg/kg dose. Thus, cytoprotection can be confirmed histol., but is limited primarily to the deep mucosa. The ability of PGE2 to enhance healing is probably related to the prevention of deep mucosal injury, which thereby allows epithelial reconstitution to occur. Lastly, the effectiveness of PGE2 as a cytoprotective agent is dose- and route-dependent.

IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(stomach damage from, PGE2 analog prevention of, administration route and dose in relation to)

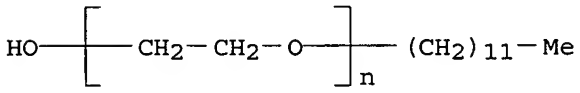
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 61 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:101252 HCAPLUS
DOCUMENT NUMBER: 108:101252
TITLE: Surfactant effects in topical drug availability
AUTHOR(S): Ashton, Paul; Hadgraft, Jonathan; Brain, Keith R.; Miller, T. Alan; Walters, Kenneth A.
CORPORATE SOURCE: Welsh Sch. Pharm., Cardiff, UK
SOURCE: International Journal of Pharmaceutics (1988), 41(3), 189-95
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of two surfactants, Na lauryl sulfate (SLS) and Brij 36T on the thermodn. activity of Me nicotinate (MN) and hexyl nicotinate (HN) in aqueous gels were investigated. In vivo, the permeability of the skin was assessed by measuring the time of onset of the erythema which is induced by these nicotinate esters. Times of onset of erythema caused by gels containing SLS correlate with the in vitro release rates suggesting that in <15 min SLS does not affect the barrier function of the skin. Results obtained for Brij 36T-containing gels, however, imply that this surfactant does increase skin permeability. SLS, normally considered to be the more powerful penetration enhancer, takes longer to exert its effect on the skin, suggesting that the 2 surfactants act on the skin in different ways.

IT 9002-92-0, Brij 36T
RL: BIOL (Biological study)
(thermodn. activity and drug release from gels in relation to)
RN 9002-92-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



L38 ANSWER 62 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:631401 HCAPLUS
DOCUMENT NUMBER: 107:231401
TITLE: Insecticide poisoning: disruption of a possible autonomic function in pupae of Tenebrio molitor
AUTHOR(S): Slama, K.; Miller, T. A.
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Prague, 15800, Czech.
SOURCE: Pesticide Biochemistry and Physiology (1987), 29(1), 25-34
CODEN: PCBPBS; ISSN: 0048-3575
DOCUMENT TYPE: Journal
LANGUAGE: English

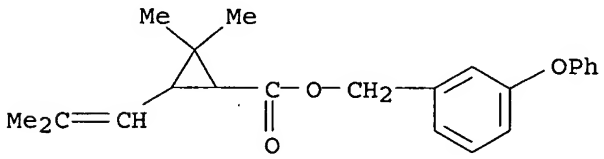
AB Poisoning of pupae of T. molitor by pyrethroid, carbamate, or organophosphate insecticides was monitored by recording pressure in the hemocoel. The pressure was controlled automatically at around a neg. 0.5 kPa value and predictable sharp peak increases in pressure of 0.5-1.0 kPa occurred in bursts. The pressure pulses in Tenebrio pupae were thought to represent the activity of an important automatic function in insects.

Insecticide poisoning increased the frequency of the pressure pulses and their amplitudes as high as 6 kPa in a dose-dependent manner. The pattern of pyrethroid-poisoned pupae was distinctly different from that following carbamate or organophosphorus poisoning. At 12-18 h after treatment, the pattern of pressure bursts in pupae recovering from poisoning began to resemble the pattern before treatment, with peaks of pressure. In pupae not recovering from poisoning, the pattern was distinctly different, with only single peak pulses of pressure. Thus, it was possible to determine the fate of poisoned pupae after 12 h.

IT 26002-80-2, Phenothrin
RL: PRP (Properties)
(Tenebrio molitor pupae poisoning by, monitoring of, by recording pressure in hemocoel)

RN 26002-80-2 HCAPLUS

CN Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, (3-phenoxyphenyl)methyl ester (9CI) (CA INDEX NAME)



L38 ANSWER 63 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:613425 HCAPLUS

DOCUMENT NUMBER: 107:213425

TITLE: Effects of ethanol and prostaglandin on rat gastric mucosal tight junctions

AUTHOR(S): Schmidt, Karmen L.; Henagan, Julia M.; Smith, Gregory S.; Miller, Thomas A.

CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA

SOURCE: Journal of Surgical Research (1987), 43(3), 253-63
CODEN: JSGRA2; ISSN: 0022-4804

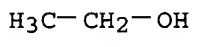
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of 16,16-dimethylprostaglandin E2 (16,16-dimethyl PGE2) upon tight junctions (TJs) of adjacent surface mucous cells (SMCs) as a possible mechanism by which prostaglandins mediate their protective effects was studied using transmission electron microscopy (TEM) and freeze fracture (FF) techniques. Fasted rats were s.c. injected with 10 μg/kg of prostaglandin (PG) or an equal volume of saline, followed 30 min later by 1 mL of oral 100% EtOH or saline. Ten or 60 min later, animals were sacrificed and stomach blocks were prepared for TEM or FF using standard techniques. Electron micrographs (+60,000) were obtained and the distance between SMC inner membrane leaflets was measured with micrometer and expressed as TJ width. Stomach blocks for FF were stored at 1°, cryoprotected, freeze fractured, and photographed by TEM (+30,000). At 0.5-μm intervals, measurements of TJ strand number and depth were made. No statistical differences were found in TJ width or strand number of SMCs among the various exptl. groups when compared with controls at each sacrifice time. At the 60 but not 10 min sacrifice time, TJ depth was greatly increased in cells treated with 10 μg/kg PG prior to EtOH exposure in contrast to control mucosa. 16,16-Dimethyl PGE2 induces no changes in the structural composition of TJs as a possible explanation for its protective properties. The increase in TJ depth observed

in EtOH-exposed mucosa following PG pretreatment at the 60 min sacrifice time is most likely related to the architectural restructuring that occurs during reconstitution of damaged surface epithelium.

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to gastric mucosal cells, prostaglandins protection from)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 64 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:569433 HCAPLUS
DOCUMENT NUMBER: 107:169433
TITLE: The protective effects of a prostaglandin without antisecretory properties against ethanol -induced injury in the rat stomach: a histologic study
AUTHOR(S): Schmidt, Karmen L.; Henagan, Julia M.; Mitchell, Philip A.; Smith, Gregory S.; Miller, T. A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Histology and Histopathology (1987), 2(2), 173-83
CODEN: HIHIES; ISSN: 0213-3911
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of 2-acetyl-2-decarboxy-15(S)-15 Me PGF2α (PGF2α) on EtOH induced injury in the rat stomach were examined to determine if a prostaglandin analog devoid of antisecretory properties could confer full or partial gastric mucosal protection. Rats were orally administered saline or PGF2α in a dose of 0.5 or 5.0 mg/kg. Thirty min later animals received varying concns. (25, 50, and 100%) of EtOH orally. Five min following EtOH exposure, they were killed and samples taken from identical regions of the glandular mucosa for microscopic evaluation. All concns. of EtOH tested damaged the gastric epithelium. The injury induced by 25% EtOH was almost exclusively confined to the surface epithelium and was not altered by either dose of PGF2α pretreatment. In contrast, both 50% and 100% EtOH elicited comparable damage to the gastric mucosa involving both the deep and superficial mucosa of virtually the entire epithelium. The deep injury induced by these 2 EtOH concns. was prevented by both the low and high dose of PGF2α. The 5.0 mg dose of PGF2α provided complete protection (i.e. both superficial and deep) to as much as 50% of the mucosa exposed to 50 or 100% EtOH. PGF2α possesses cytoprotective dose-related properties involving both the superficial and deep epithelium.

L38 ANSWER 65 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:115267 HCAPLUS
DOCUMENT NUMBER: 106:115267
TITLE: Long-acting pyrethrum/pyrethroid based pesticides with silicone stabilizers
INVENTOR(S): Allan, Graham G.; Miller, Thomas A.
PATENT ASSIGNEE(S): Adams Veterinary Research Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8603374	A1	19860619	WO 1985-US2386	19851204 <--
W: GB, JP				
US 4668666	A	19870526	US 1984-678404	19841205 <--
JP 62500935	T2	19870416	JP 1986-500135	19851204 <--
GB 2181648	A1	19870429	GB 1986-18267	19861204 <--
GB 2181648	B2	19880817		

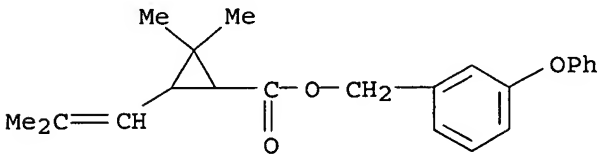
PRIORITY APPLN. INFO.: US 1984-678404 A 19841205
WO 1985-US2386 W 19851204

AB Alkylarylsilicones, especially tetramethyltetraphenylsiloxane, prolong the life-time of compns. containing pyrethrum, pyrethroids and synergists. Thus, a formulation containing pyrethrum 0.10, piperonyl butoxide 0.37, octylbicycloheptene dicarboximide, 0.61, 2,3,4,5-bis(2-butylene)tetrahydro-2-furaldehyde 0.20, di-Pr isocinchomeronate 0.20, 2-ethylhexyl p-dimethylaminobenzoate 0.25, 2-ethylhexyl 2-cyano-3.3-diphenylacrylate 0.25, butylated hydroxytoluene 0.20, tetramethyltetraphenyltrisiloxane 0.51, petroleum distillate 0,4, fragrance oil 0.40 and iso-PrOH 96,51% had a prolonged action, killing dog fleas (Ctenocephalides) and ticks (Rhipicephalus). Using pyrethrum alone, the killing action is very short-lived.

IT 26002-80-2, Phenothrin
RL: BIOL (Biological study)
(insecticidal composition containing silicone stabilizer and)

RN 26002-80-2 HCAPLUS

CN Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, (3-phenoxyphenyl)methyl ester (9CI) (CA INDEX NAME)



L38 ANSWER 66 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:82133 HCAPLUS
DOCUMENT NUMBER: 106:82133
TITLE: Maturational changes in the pharmacological characteristics and actomyosin content of canine arterial and venous tissue
AUTHOR(S): Seidel, C. L.; Ross, B.; Michael, L.; Freedman, J.; Burdick, B.; Miller, T.
CORPORATE SOURCE: Dep. Med. Physiol., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Pediatric Research (1987), 21(2), 152-8
CODEN: PEREBL; ISSN: 0031-3998
DOCUMENT TYPE: Journal
LANGUAGE: English

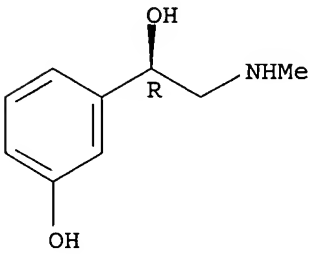
AB The purpose of this study was to compare the pharmacol. characteristics and actomyosin content of arterial and venous tissue at different times during development. Rings of arteries (femoral, renal, carotid, and pulmonary) and veins (saphenous, pulmonary, and jugular) were obtained from 1 wk, 1 mo, and adult dogs and mounted at their optimal length for

force development, and the contractile response to KCl and phenylephrine determined The strain at optimal length was less at all ages in pulmonary artery and pulmonary and jugular veins than in other vessels. All vessels exhibited an increase in maximum contractile response with development, but the increase was greater for phenylephrine. In general, the magnitude of the maximum response of the jugular and pulmonary veins and pulmonary artery was less than that of other vessels at all ages. The sensitivity (half maximum response) either increased or was unchanged in arteries with development, whereas in the veins it either decreased or was unchanged. The relaxant effects of verapamil and isoproterenol (I) were determined on KCl-contracted vessels. Arterial tissue was minimally responsive to I at all ages, whereas venous tissue either increased its responsiveness (saphenous and pulmonary) with development or remained highly responsive (jugular). Verapamil, unlike I, was an effective relaxant of all vessels. The actomyosin content of femoral and renal arteries and saphenous and jugular veins increased with development, but this increase was accompanied by a parallel increase in total protein so that the ratio (actomyosin/total protein) was unchanged. In jugular veins from adult dogs this ratio was smaller than that in arterial tissue. Apparently, arterial and venous tissues increase their maximum contractile response during maturation. Because the maximum response to agents with different mechanisms of action (KCl and phenylephrine) increased at different rates, the increase must be due to more than a quant. increase in contractile material, possibly to differences in the rate of maturation of their resp. excitation-contraction coupling processes. However, when maturational changes in other characteristics are compared, differences are observed between arteries and veins as well as between vessels within a given class, indicating intervessel heterogeneity in maturation.

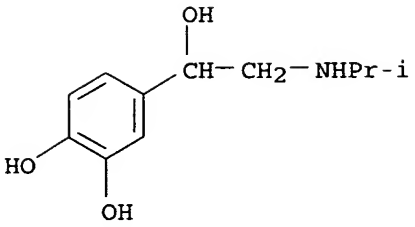
IT 59-42-7, Phenylephrine 7683-59-2
RL: BIOL (Biological study)
(artery and vein contraction response to, in development, actomyosin content in relation to)

RN 59-42-7 HCAPLUS
CN Benzenemethanol, 3-hydroxy-α-[(methylamino)methyl]-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 7683-59-2 HCAPLUS
CN 1,2-Benzenediol, 4-[1-hydroxy-2-[(1-methylethyl)amino]ethyl]- (9CI) (CA INDEX NAME)



L38 ANSWER 67 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:61750 HCAPLUS
DOCUMENT NUMBER: 106:61750
TITLE: N-acetylcysteine and prostaglandin. Comparable protection against experimental ethanol injury in the stomach independent of mucus thickness
AUTHOR(S): Henagan, Julia M.; Smith, Gregory S.; Miller, Thomas A.; Schmidt, Karmen L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Annals of Surgery (1986), 204(6), 698-704
CODEN: ANSUA5; ISSN: 0003-4932
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of barrier mucus in mediating the protective effects of 16,16-dimethyl-PGE2 (dm-PGE2) [39746-25-3] against EtOH [64-17-5]-induced gastric injury, with and without concomitant treatment with N-acetylcysteine (NAC) [616-91-1], a potent mucolytic agent, was evaluated. Fasted rats were orally administered saline, dm-PGE2 NAC, or dm-PGE2 plus NAC. In the 1st study, the rats were killed 15 min later and their stomachs were removed and assayed for barrier mucus adherent to the gastric wall by the Alcian blue technique. In the 2nd study, the rats were orally given 2 mL of EtOH after receiving 1 of these pretreatment regimens, and 5 min later they were killed and their stomachs were evaluated histol. by light microscopy for the magnitude of EtOH injury. Although NAC reduced the thickness of barrier mucus by 76% when compared with control animals, it did not adversely affect the ability of dm-PGE2 to spare the deep epithelium from injury by EtOH. In fact, NAC was as effective a protective agent as dm-PGE2. Neither agent prevented damage to the surface epithelium by EtOH, which verifies previous studies regarding the protective effects of prostaglandins. Thus, both dm-PGE2 and NAC prevent EtOH-induced damage to the deeper layers of the gastric mucosa independent of mucus gel layer thickness, this suggests that mechanisms other than mucus are involved in mediating this protection.
IT 64-17-5, Ethanol, biological studies
RL: PRP (Properties)
(toxicity of, to stomach mucosa, acetylcysteine and prostaglandin prevention of)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 68 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:1048 HCAPLUS
DOCUMENT NUMBER: 106:1048

TITLE: Influence of prostaglandin on repair of rat stomach damaged by absolute ethanol
AUTHOR(S): Schmidt, Karmen L.; Bellard, R. Lane; Smith, Gregory S.; Henagan, Julia M.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Journal of Surgical Research (1986), 41(4), 367-77
CODEN: JSGRA2; ISSN: 0022-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The possible role that prostaglandins (PGs) may play in enhancing epithelial repair in EtOH [64-17-5]-damaged gastric mucosa was examined Fasted rats were injected s.c. with 10 μg/kg of 16,16-dimethyl PGE2 [39746-25-3] or saline and 30 min later received an oral bolus of 1 mL of absolute EtOH or saline. At 5 min and 2, 8, and 24 h after EtOH exposure tissues were prepared from identical regions of the glandular mucosa for microscopic evaluation. Normal, injured, and repairing tissues were differentiated and quantitated. The length of injured surface epithelium was the same in EtOH-treated tissues with and without PG pretreatment when evaluated 5 min after EtOH exposure, but the deeper epithelium was protected from injury in animals receiving PG pretreatment. Although the repair process itself was identical in the 2 exptl. groups, in PG-treated tissues repair was initiated earlier, was more widespread, and was much more rapid than in tissues exposed to EtOH without such treatment. At the end of 24 h of observation, only 5.5% of the surface epithelium was considered normal histol. in mucosa exposed to EtOH alone without PG pretreatment. This is in marked contrast to PG-treated tissues in which 82.7% of the gastric surface was normal at 24 h. The mechanism responsible for these findings is unknown but may be related to PG's ability to spare the cellular pool in the gland isthmus from damage, enhancement of cellular migration from this pool to resurface the damaged epithelium, or a combination of both of these processes.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(stomach lesions from, PGE2 analog protection against)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 69 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:532733 HCAPLUS
DOCUMENT NUMBER: 105:132733
TITLE: Dietary fat and cholesterol modification of rat abdominal aorta prostacyclin and leukotriene production (in vitro)
AUTHOR(S): Blankenship, J. W.; Miller, T.; Boucek, R. J.
CORPORATE SOURCE: Dep. Nutr. Sch. Health, Loma Linda Univ., Loma Linda, CA, 92350, USA
SOURCE: Prostaglandins, Leukotrienes and Medicine (1986), 23(1), 45-52
CODEN: PLMEDD; ISSN: 0262-1746
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Groups of weanling male Sprague-Dawley rats fed formulated diets containing 15% by weight of corn oil (CO), linseed oil (LNO), or CO + 1% cholesterol [

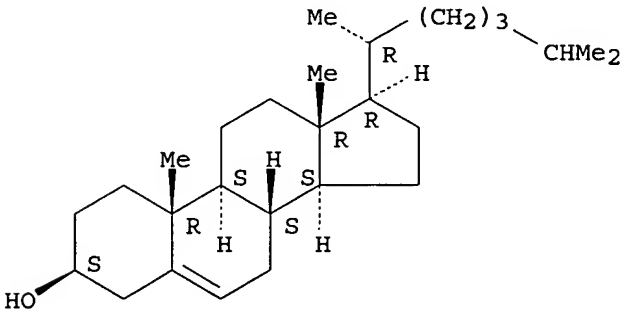
57-88-5] and 0.25% cholic acid (CH-CH) were sacrificed after 8 wk and the aortas removed. Three mm length cross-sectional rings were cut from the distal abdominal aorta segment and incubated in either Tris buffer (pH 7.4, 37°, 10 min) for measurements of prostacyclin as 6-keto-prostaglandin F1α (6-keto-PGF1α) [58962-34-8] or Tris buffer plus 10 μM ionophore A23187 for measurement of leukotriene C4 (LTC4) [72025-60-6] production using radioimmunoassay procedures. 6-Keto-PGF1α production was greater in the CO than in the LNO and CH-CH fed rats by 54 and 40%, resp. LNO diets significantly lowered LTC4 production when compared to tissues from CO-fed rats. LTC4 production by tissues from the CH-CH-fed animals was lower than tissues from CO-fed animals; however, the difference failed to reach levels of significance because of data spread and the number of tissues. Tissues from the CH-CH-fed and LNO-fed rats were significantly different than those of the CO since LTC4 formation was high relative to 6-keto-PGF1α production These results suggest distinctive effects of dietary fat and cholesterol on the syntheses of vasoactive eicosanoids that may be relevant to arterial tissue physiol. and pathol.

IT 57-88-5, biological studies
RL: BIOL (Biological study)
(aorta leukotrienes and prostacyclins response to dietary)

RN 57-88-5 HCAPLUS

CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 70 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:501367 HCAPLUS

DOCUMENT NUMBER: 103:101367

TITLE: Assays for biogenic amines in insect nervous tissue

AUTHOR(S): Evans, P. D.; Davenport, A. P.; Elias, M. S.; Morton, D. B.; Trimmer, B. A.

CORPORATE SOURCE: Univ. Cambridge, Cambridge, UK

SOURCE: Neurochem. Tech. Insect Res. (1985), 25-46.
Editor(s): Breer, Heinz; Miller, Thomas A.
Springer: Berlin, Fed. Rep. Ger.
CODEN: 53SWA4

DOCUMENT TYPE: Conference

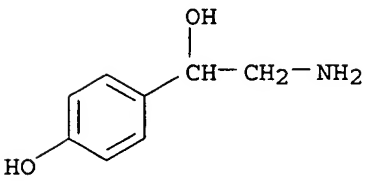
LANGUAGE: English

AB Radioenzymic assays are described for octopamine, dopamine, noradrenaline, 5-HT, and histamine in insect nervous tissue. HPLC of biogenic amines is also described.

IT 104-14-3
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in insect nervous tissue by radioenzymic assay)

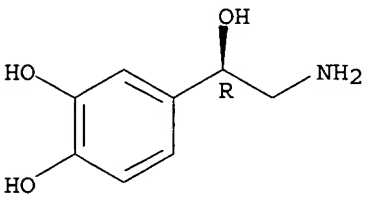
RN 104-14-3 HCAPLUS

CN Benzenemethanol, α-(aminomethyl)-4-hydroxy- (9CI) (CA INDEX NAME)



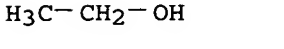
IT 51-41-2
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in insect nervous tissue by radioenzymic assay or HPLC)
RN 51-41-2 HCAPLUS
CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L38 ANSWER 71 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:499382 HCAPLUS
DOCUMENT NUMBER: 103:99382
TITLE: Nonprotein sulfhydryl compounds in canine gastric mucosa: effects of PGE2 and ethanol
AUTHOR(S): Miller, Thomas A.; Li, Donghui; Kuo, Yuh Jyh; Schmidt, Karmen L.; Shanbour, Linda L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1985), 249(1, Pt. 1), G137-G144
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By use of an in vivo canine chambered stomach preparation in which the gastric mucosa was partitioned into 2 equal halves, the effect of topical 16,16-dimethyl PGE2 (DMPGE2) [39746-25-3] (1 μg/mL of perfusate) and 8% and 40% EtOH on tissue levels of nonprotein sulfhydryl compds. was assessed. Both DMPGE2 and 8% EtOH significantly increased mucosal levels of nonprotein sulfhydryls when compared with corresponding mucosa bathed with saline alone. In contrast, mucosa bathed with 40% EtOH showed significantly decreased levels. If mucosa was bathed with DMPGE2 or 8% EtOH prior to exposing the stomach to 40% EtOH, this depletion in sulfhydryl compds. was not observed Since other exptl. observations have shown that exogenously administered prostaglandins and mild irritants (such as low-dose alc.) can prevent gastric mucosal damage by necrotizing agents (such as high-dose alc.), findings are consistent with the hypothesis that nonprotein sulfhydryls play a role in mediating gastric mucosal protection.
IT 64-17-5, biological studies
RL: BIOL (Biological study)
(nonprotein sulfhydryl compds. of stomach mucosa response to)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 72 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:190996 HCAPLUS
DOCUMENT NUMBER: 102:190996
TITLE: Physical and chemical characteristics of some high purity magnesium stearate and palmitate powders
AUTHOR(S): Miller, T. A.; York, P.
CORPORATE SOURCE: Postgrad. Sch. Stud. Pharm., Univ. Bradford, Bradford, BD7 1DP, UK
SOURCE: International Journal of Pharmaceutics (1985), 23(1), 55-67
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High-purity Mg stearate [557-04-0] and Mg palmitate [2601-98-1] powders were prepared at 2 batch sizes under different pH environments. Larger batch products were analyzed for chemical and phys. character using gas chromatog., atomic absorption, surface area estimation, SEM, thermal anal. (moisture evolution anal., DSC, thermogravimetric anal., hot stage microscopy), IR and x-ray diffraction techniques. Powder particles produced under acid conditions had a thin, regular, plate-like appearance whereas those manufactured from alkaline conditions had more irregular structure. Acid-manufactured powders were associated with 2 mols. of water and had a small degree of structure which was disrupted on drying. Materials precipitated from alkaline conditions appeared to consist of 2 species, the major 1 being 1 mol. of Mg stearate or palmitate associated with 2 mols. of water, and the 2nd minor component probably associated with equimolar proportions of water. Ests. of activation energy associated with the major thermal transitions confirmed the low level mol. structure in prepared materials.

L38 ANSWER 73 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:161130 HCAPLUS
DOCUMENT NUMBER: 102:161130
TITLE: Failure of 16,16-dimethyl PGE2 to prevent inhibitory effect of ethanol on sodium transport in canine gastric mucosa
AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.; Kuo, Yuh Jyh; Shanbour, Linda L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: American Journal of Physiology (1985), 248(3, Pt. 1), G299-G306
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An in vitro canine gastric mucosal preparation was used to evaluate the effects of EtOH [64-17-5] (2, 4, 6, and 8%) and indomethacin (2.2 + 10-4M), with and without 16,16-dimethyl-PGE2 (I) [39746-25-3] pretreatment, on net Na+ transport (JnetNa) (mucosal to serosal) across gastric epithelium. Although administration of 2 or 4% EtOH to the mucosal bathing solution had no appreciable inhibitory effects on Na+

transport, 6 and 8% EtOH and indomethacin inhibited JnetNa when compared with untreated control mucosa. This effect was accompanied by inhibition of transmucosal p.d. and short-circuit current (Isc). In other mucosae exposed to I (8 + 10-6M) in the serosal bathing solution, increases in JnetNa, p.d., and Isc were noted when compared with control mucosa. Addition of 6 or 8% EtOH to the mucosal solution of I-pretreated tissue resulted in decreases in p.d., Isc, and JnetNa below control values that were not different from mucosa exposed to 6 and 8% EtOH without I pretreatment. When indomethacin was added to the mucosal solution following I pretreatment, only slight decreases in p.d. and Isc below control levels were observed, and the inhibitory effects on JnetNa induced by indomethacin without such treatment were abolished. I stimulation of JnetNa may thus play a role in its ability to prevent indomethacin damage to gastric epithelium but does not appear to be of importance in mediating protection against EtOH damage.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(sodium transport by gastric mucosa inhibition by, PGE2 analog effect on)

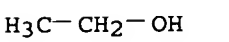
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

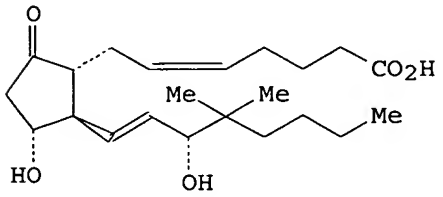
L38 ANSWER 74 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:143820 HCAPLUS
DOCUMENT NUMBER: 102:143820
TITLE: Prostaglandin cytoprotection against ethanol -induced gastric injury in the rat. A histologic and cytologic study
AUTHOR(S): Schmidt, Karmen L.; Henagan, Julia M.; Smith, Gregory S.; Hilburn, Pamela J.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Gastroenterology (1985), 88(3), 649-59
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Time-sequence study light microscopy, SEM, and TEM were used to evaluate the effects of 16,16-dimethyl-PGE2 (I) [39746-25-3] on gastric mucosal integrity after exposure to 100% EtOH [64-17-5]. Macroscopically, virtually complete protection against injury to the glandular mucosa of the in vivo rat stomach was noted in animals receiving 10 μg/kg of I s.c. before oral EtOH administration when killed at 5, 20, and 60 min after EtOH exposure compared with oral EtOH after saline injection. On light microscopy the length of injured epithelium in I/EtOH- and saline/EtOH-treated tissues was not significantly different at all time periods studied. Although the depth of injury extended into gastric glands in both groups killed at 5 min, the deep pit surface mucus cells in I/EtOH mucosa were less damaged and necrotic lesions were virtually absent when compared with saline/EtOH mucosa. At 20 and 60 min, cellular injury could still be identified in I/EtOH-treated mucosa but the depth of injury became even less pronounced over time in contrast to mucosa exposed to EtOH without I. SEM and TEM confirmed these differences. Apparently, I does not prevent superficial surface mucus cell necrosis in EtOH-exposed mucosa even though it does spare cells in the pit base. The repithelialization of the lamina propria may be initiated by spared deep-lying pit cells.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(stomach damage from, dimethyl-PGE2 prevention of)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



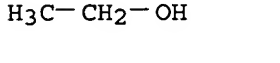
L38 ANSWER 75 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:19391 HCAPLUS
DOCUMENT NUMBER: 102:19391
TITLE: Influence of vagotomy on mucosal protection against alcohol-induced gastric damage in the rat
AUTHOR(S): Henagan, Julia M.; Smith, Gregory S.; Seidel, Edward R.; Miller, Thomas A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Gastroenterology (1984), 87(4), 903-8
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

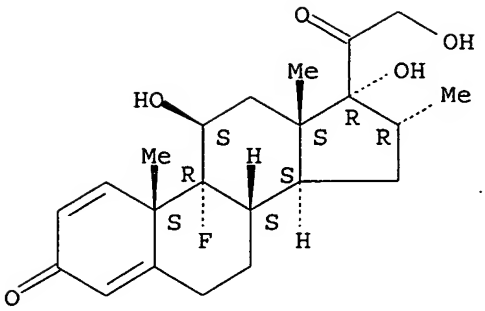
AB The role of the vagus nerve in mediating the protective effects of s.c. 16,16-di-Me prostaglandin E2 (I) [39746-25-3] or the mild irritant 30% EtOH [64-17-5] (topically) against gastric mucosal injury induced by concentrated solns. of EtOH was examined Anesthetized rats underwent either truncal vagotomy or sham truncal vagotomy and studied acutely or 7 days later. Under acute conditions, in rats with intact vagi, oral saline followed by 100% EtOH produced severe gastric hemorrhagic and necrotic lesions throughout the glandular gastric mucosa. Oral 30% EtOH or pretreatment with I (5, 10, or 25 μg/kg) before giving oral saline significantly reduced the magnitude of injury when mucosa subsequently exposed to 100% EtOH. In animals with truncal vagotomy, the protective effect of I or 30% EtOH was not observed Similar results were noted when animals were studied 7 days after sham or truncal vagotomy. In other studies, the ability of I to prevent gastric injury induced by 50% EtOH or 80 mM aspirin [50-78-2] in acid solution 160 mM HCl with and without prior vagotomy was compared. Although I (5 or 25 μg/kg) pretreatment significantly reduced the degree of gastric damage induced by the agents in the nonvagotomized state, and by aspirin under vagotomized conditions, only partial protection by I against EtOH injury was observed in the vagotomized state. Apparently, the mechanisms whereby prostaglandins mediate their protective effects against aspirin and EtOH may be different and the vagus nerve influences the ability of I and the mild irritant 30% EtOH to prevent alc.-induced injury in the rat stomach.

IT 64-17-5, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to gastric mucosa, di-Me PGE2 protection against, vagotomy in relation to)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

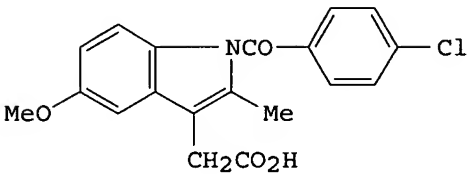


L38 ANSWER 76 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:584339 HCAPLUS
DOCUMENT NUMBER: 101:184339
TITLE: Evidence for microheterogeneity in the structure of human glucocorticoid receptors
AUTHOR(S): Cidlowski, John A.; Richon, Victoria
CORPORATE SOURCE: Dep. Physiol., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Endocrinology (1984), 115(4), 1588-97
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human glucocorticoid receptor has been selectively affinity-labeled with 3H-labeled dexamethasone [50-02-2] by utilizing whole cells to form complexes of steroids and receptors. The nonspecific interaction of [3H]dexamethasone mesylate ([3H]DM) with proteins containing sulfhydryl groups has been minimized by incubation of intact HeLa S3 cells with 1 + 10-8 M [3H]DM at 0° before preparation of cytosol fractions. Under these conditions, which result in the labeling of 30% of the total cellular receptor, [3H]DM binds to a protein that has a mol. weight of about 88,000 and which apparently represents the glucocorticoid receptor. [3H]DM binding is saturable. Glucocorticoids and progesterone, but not estradiol or testosterone, compete with [3H]DM for binding with the 88,000-dalton protein. The sedimentation behavior of the glucocorticoid receptors is quite similar whether they are labeled with [3H]DM or with [3H]dexamethasone. Protein labeled with [3H]DM sediments as an approx. 7.5S species in 5-20% sucrose gradients. Increasing the ionic strength of the buffer during centrifugation produces a receptor form that sediments as a species at about 4.5S. The affinity labeled glucocorticoid receptors display isoelec. focusing patterns nearly identical to those observed for receptors labeled with [3H] dexamethasone. [3H]DM-receptor complexes have been subjected to high resolution 2-dimensional gel anal. The human glucocorticoid receptor apparently consists of a family of at least 5 proteins with mol. masses of approx. 88,000 which have discrete isoelec. points ranging from 6.5-7.5. This heterogeneous population of proteins may represent multiple species of steroid receptor proteins within the same cell or perhaps post-transcriptional modification of a single protein.
IT 50-02-2
RL: BIOL (Biological study)
(receptors for, of human, protein microheterogeneity in relation to)
RN 50-02-2 HCAPLUS
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



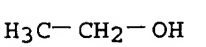
L38 ANSWER 77 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:134102 HCAPLUS
DOCUMENT NUMBER: 100:134102
TITLE: Indomethacin decreases resistance of gastric barrier to disruption by alcohol
AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1984), 29(2), 141-9
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



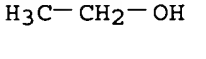
I

AB Using a canine chambered stomach preparation, the effects of 3 30-min exposures of the gastric mucosa to 20% EtOH [64-17-5] in 100 mN HCl on gastric mucosal barrier disruption and ulcer formation were assessed. The interval between exposures was 30 min. Following an initial exposure to 20% EtOH, the net fluxes of H+, Na+, and K+ ions and perfusate volume induced by a 2nd and 3rd exposure of the gastric epithelium to alc . were reduced. Only minimal ulceration was observed following the 1st exposure which did not worsen with subsequent exposure to EtOH. If indomethacin (I) [53-86-1] was given i.v. either before or immediately after the 1st EtOH exposure, recovery of barrier function was lessened after this challenge, and the resistance to barrier disruption was decreased during the 2 subsequent exposures to EtOH when compared to expts. in which mucosa was exposed to 20% EtOH without concomitant administration of I. In addition, marked mucosal ulceration was observed during the 2nd and 3rd EtOH exposures if I was given. Probably, the 1st alc. challenge elicited the synthesis and release of tissue prostaglandins and thereby enhanced resistance of the gastric mucosa to subsequent challenge by this damage agent. When prostaglandin synthesis was blocked by I, the increased resistance to gastric injury did not occur.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(gastric damage from, indomethacin effect on)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 78 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:115492 HCAPLUS
DOCUMENT NUMBER: 100:115492
TITLE: Role of sodium transport in prostaglandin cytoprotection
AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.; Kuo, Yuh Jyh; Shanbour, Linda L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Mech. Mucosal Prot. Upper Gastrointest. Tract (1984), 357-63. Editor(s): Allen, Adrian. Raven: New York, N. Y.
CODEN: 50WXA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB EtOH [64-17-5] and indomethacin [53-86-1] inhibited active Na transport by isolated canine mucosa strips. However, 16,16-dimethyl-PGE2 [39746-25-3] stimulated basal Na transport and prevented indomethacin-induced inhibition of ion transport. EtOH-induced Na transport inhibition was unaffected by the prostaglandin. The possible role of Na transport in prostaglandin cytoprotection is discussed.
IT 64-17-5, biological studies
RL: BIOL (Biological study)
(sodium transport by stomach inhibition by, prostaglandin effect on, cytoprotection in relation to)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 79 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:1974 HCAPLUS
DOCUMENT NUMBER: 100:1974
TITLE: Indomethacin prevents resistance to alcohol -induced gastric mucosal damage
AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Surgical Forum (1982), 33, 156-9
CODEN: SUFOAX; ISSN: 0071-8041
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When the exteriorized gastric mucosa of dogs was bathed with 20% EtOH [64-17-5] in situ for 3 30-min periods interspersed with 30-min rest periods, the 1st exposure reduced the net fluxes of H+ and K+ ions induced by the 2nd and 3rd exposures. Na+ flux was not significantly altered and only minimal ulcer formation occurred. Indomethacin [53-86-1] (10 mg/kg as an i.v. bolus followed by 3 mg/kg/h as a continuous

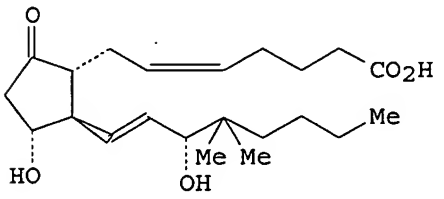
infusion) prevented this resistance to barrier disruption and induced ulceration of the mucosa. Indomethacin alone had no effect on barrier function and produced no ulceration. Thus, the 1st alc. exposure may have elicited the synthesis and release of tissue prostaglandins and enhanced resistance of the gastric mucosa to subsequent exposure.

IT 64-17-5, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to gastric mucosa, indomethacin effect on)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 80 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:593714 HCAPLUS
DOCUMENT NUMBER: 97:193714
TITLE: Prostaglandin prevents alterations in DNA, RNA, and protein in damaged gastric mucosa
AUTHOR(S): Miller, Thomas A.; Gum, Elizabeth T.; Guinn, Edward J.; Henagan, Julia M.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Digestive Diseases and Sciences (1982), 27(9), 776-81
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB In rats, gastric mucosal damage by absolute EtOH [64-17-5] administration and the associated decreases in tissues of DNA, RNA, and protein were prevented by pretreatment with 16,16-dimethyl-PGE2 (I) [39746-25-3] (1 μg/kg, s.c.). I had no effect on tissue levels of DNA, RNA, and protein in animals not exposed to alc. DNA synthesis in the mucosa was the same in all groups of rats studied. Thus, I maintains normal tissue levels of nucleic acids and proteins by preventing shedding of mucosal cells, and the ability of I to prevent gastric damage by alc. is not mediated through stimulation of DNA synthesis.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(stomach mucosa damage from, nucleic acid and protein decrease in, dimethyl-PGE2 prevention of)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

L38 ANSWER 81 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:435882 HCAPLUS
DOCUMENT NUMBER: 95:35882
TITLE: Aminergic and peptidergic receptors at the heart muscle of Locusta migratoria migratorioides R.F.
AUTHOR(S): Saghy-Rozsa, Katalin; Miller, T. A.
CORPORATE SOURCE: Biol. Res. Inst., Hung. Acad. Sci., Tihany, Hung.
SOURCE: Adv. Physiol. Sci., Proc. Int. Congr., 28th (1981), Meeting Date 1980, Volume 22, Issue Neurotransm. Invertebr., 557-81. Editor(s): S.-Rozsa, K. Akad. Kiado: Budapest, Hung.
CODEN: 45TGAW
DOCUMENT TYPE: Conference
LANGUAGE: English

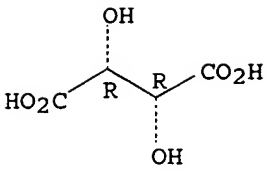
AB The effect of aminergic and peptidergic neurotransmitters was studied on semi-isolated and isolated heart prepns. from L. migratoria. Acetylcholine chloride (ACh) [60-31-1], l-noradrenaline bitartrate (NA) [51-40-1], 5-hydroxytryptamine creatinine sulfate (5-HT) [971-74-4], dopamine-HCl (DA) [62-31-7], and D,L-octopamine-HCl (DP) [770-05-8] all increased spontaneous action potential of heart muscle. The effect of ACh was blocked by d-tubocurarine, nicotine, and atropine. 5-HT effect was eliminated completely by BDL-148 and partially inhibited by methylsergide. Both bicuculline and picrotoxin antagonized the inhibitory action of GABA [56-12-2] on the heart. OP effect was inhibited by 5-methoxygramine. Proctolin [57966-42-4] had a biphasic action on heart muscle being stimulatory at low and inhibitory at high concns. The effects of proctolin were additive with those of 5 HT. α-Ecdysone [3604-87-3] had an equivalent effect to that of proctolin whereas β-ecdysone [5289-74-7] was less potent. CAMP [60-92-4] of heart was increased by the neurotransmitters with the following order of potency: OP > DA > NA > 5-HT > proctolin. L-Aspartate [56-84-8] and L-glutamate [56-86-0] were ineffective in this preparation Crude exts. of locust brain produced consistent contraction of the diaphragm and heart but the pure neurotransmitters had no effect on alary muscle. Apparently, circulating hormones may be involved in heart regulation in the locust and their effects may be long lasting.

IT 51-40-1 770-05-8
RL: BIOL (Biological study)
(heart muscle contraction stimulation by, in locust, receptors in relation to)
RN 51-40-1 HCAPLUS
CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 87-69-4
CMF C4 H6 O6

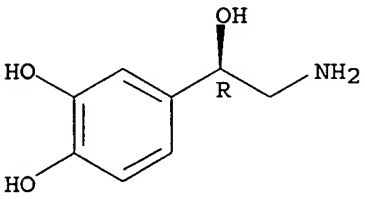
Absolute stereochemistry.



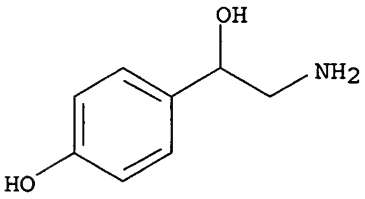
CM 2

CRN 51-41-2
CMF C8 H11 N O3

Absolute stereochemistry. Rotation (-).

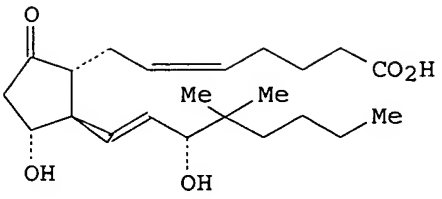


RN 770-05-8 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)-4-hydroxy-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L38 ANSWER 82 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:186013 HCAPLUS
DOCUMENT NUMBER: 94:186013
TITLE: Topical 16,16-dimethyl PGE2 prevents alcohol -induced damage in canine gastric mucosa
AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: Surgery (St. Louis) (1981), 89(4), 494-9
CODEN: SURGAZ; ISSN: 0039-6060
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



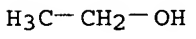
I

AB Irrigation of canine Heidenhain pouches with EtOH [64-17-5] in acid solution damaged gastric mucosa, as was evidenced by large increases in net fluxes of Na+ and K+ into the pouch, loss of H+ from the bathing solution, and an increase in gastric perfusate volume Topical application to the pouches of 16,16-dimethyl PGE2 (I) [39746-25-3] had no effect on H+ or K+ fluxes but increased Na+ flux and volume output. Pretreatment of the pouches with topical I before EtOH prevented alc.-induced mucosal damage associated with antagonism of the changes in K+ flux and H+ loss induced by EtOH alone. The antiulcer effect of I may be due to its ability to stimulate an increase in gastric perfusate volume rich in Na which prevents permeation of H+ through the mucosa.

IT 64-17-5, biological studies
RL: BIOL (Biological study)
(gastric mucosa damage from, di-Me PGE2 prevention of)

RN 64-17-5 HCAPLUS

CN Ethanol (9CI) (CA INDEX NAME)



L38 ANSWER 83 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:438399 HCAPLUS

DOCUMENT NUMBER: 93:38399

TITLE: Octopamine and proctolin mimic spontaneous membrane depolarization in Lucilia larvae

AUTHOR(S): Irving, S. N.; Miller, T. A.

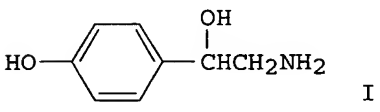
CORPORATE SOURCE: Dep. Entomol., Univ. California, Riverside, CA, 92521, USA

SOURCE: Experientia (1980), 36(5), 566-8
CODEN: EXPEAM; ISSN: 0014-4754

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

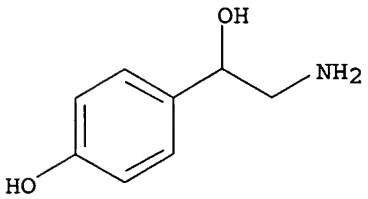
AB DL-Octopamine-HCl (I-HCl) [770-05-8] or proctolin [57966-42-4] produced rhythmic membrane depolarizations of L. sericata larvae body wall muscles that were similar to the spontaneous depolarizations observed in such tissues. The effects of I and proctolin were not abolished by the axonal conduction blocker tetrodotoxin or by agonists for the fast or slow axon

receptors. Rhythmic depolarizations were apparently induced by a postsynaptic action, and this effect may be Ca dependent. Muscles sensitive to I were insensitive to proctolin, and vice versa, indicating that the responses were mediated by sep. receptors for each substance.

IT 770-05-8
RL: PRP (Properties)
(membrane depolarization by, in muscle of Lucilia sericata larvae)

RN 770-05-8 HCAPLUS

CN Benzenemethanol, α-(aminomethyl)-4-hydroxy-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L38 ANSWER 84 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:16144 HCAPLUS

DOCUMENT NUMBER: 92:16144

TITLE: Protection against alcohol-induced gastric mucosal damage by topical prostaglandin E2

AUTHOR(S): Miller, Thomas A.; Henagan, Julia M.

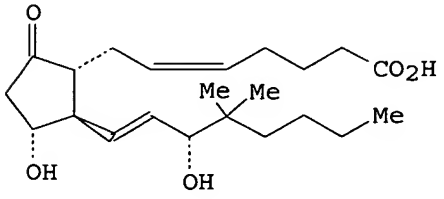
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA

SOURCE: Surgical Forum (1979), 30, 334-7
CODEN: SUFOAX; ISSN: 0071-8041

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



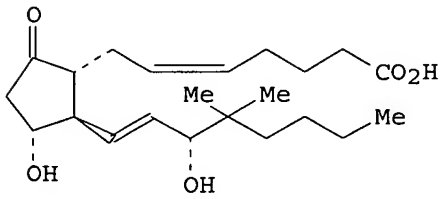
I

AB Topical application of 16,16-dimethylprostaglandin E2 (I) [39746-25-3] to the gastric epithelium of dogs with Heidenhain pouches prevented epithelial damage induced by EtOH [64-17-5], such damage being characterized by large fluxes of Na+ and K+ into the pouch, loss of H+ from the bathing solution, and an increase in the gastric perfusate volume Although I by itself did increase Na+ flux and volume output, these effects were not increased further in the presence of EtOH. I alone had no effect on H+ and K+ fluxes, and it completely prevented the changes induced by EtOH.

IT 64-17-5, biological studies

RL: PRP (Properties)
(toxicity of, to stomach, prostaglandins effect on)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

L38 ANSWER 85 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:34385 HCAPLUS
DOCUMENT NUMBER: 90:34385
TITLE: Effect of 16,16-dimethyl prostaglandin E2 on ethanol-induced damage to canine oxyntic mucosa
AUTHOR(S): Tepperman, Barry L.; Miller, Thomas A.; Johnson, Leonard R.
CORPORATE SOURCE: Dep. Physiol., Univ. Texas Med. Sch., Houston, TX, USA
SOURCE: Gastroenterology (1978), 75(6), 1061-5
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

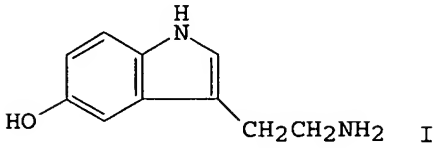


I

AB Using the canine Heidenhain pouch, action of 16,16-dimethylprostaglandin E2 (I) [39746-25-3] on gastric mucosal damage induced by 15% EtOH [64-17-5] both in the presence and absence of HCl was studied. EtOH by itself damaged the pouches as evidenced by large net fluxes of Na+ and K+ into the pouch. The combination of EtOH and 100 mN HCl produced the same effects on Na+ and K+ and also increased pepsin secretion into the pouch and the loss of H+ from the bathing solution I.v. injection of I (0.01, 0.1, and 1.0 μg/kg), 1/2 h before administration of EtOH in acid solution, decreased the net loss of H+ from the pouch and the gain of Na+, K+, and pepsin. The most EDs for protection were 0.1 and 1.0 μg/kg. The increases in Na+ and K+ efflux elicited by EtOH in the absence of HCl were also decreased by I. Thus, I effectively protects the canine gastric mucosa against the damaging effects of alc. and this protection is dose-related. The mechanism of this effect appears to be independent of inhibition of acid secretion because equal protection against EtOH was observed in the presence and absence of HCl.
IT 64-17-5, biological studies
RL: BIOL (Biological study)
(stomach mucosa damage from, PGE2 analog effect on)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

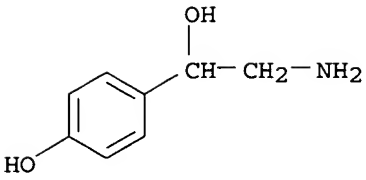
L38 ANSWER 86 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:463065 HCAPLUS
DOCUMENT NUMBER: 87:63065
TITLE: Studies on the action of biogenic amines on cockroach heart
AUTHOR(S): Collins, C.; Miller, T.
CORPORATE SOURCE: Dep. Entomol., Univ. California, Riverside, CA, USA
SOURCE: Journal of Experimental Biology (1977), 67, 1-15
CODEN: JEBIAM; ISSN: 0022-0949
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The whole abdominal heart of large nymphs or adult cockroaches responded to low concns. of acetylcholine (ACh) [51-84-3] or 5-hydroxytryptamine (I) [50-67-9] by increasing the rate of the heart beat. Prepns., which included 2-chamber sections of the abdominal heart, showed vastly decreased responses to ACh compared to the responses of the whole abdominal heart. Responses to I were similar in both prepns. Following assay with I, the cockroach heart beat often developed marked regularity. ACh assays produced such regularity only rarely. The sectioned cockroach heart preparation was decreasingly responsive to I > synephrine [94-07-5] > octopamine [104-14-3] > tryptamine [61-54-1] > dopamine [51-61-6] > tyramine [51-67-2]. Dose-response curves revealed that the antagonist 501 c interacted competitively with I on the cockroach heart preparation 501 C appeared to be a noncompetitive antagonist to octopamine, suggesting that I and octopamine act at sep. receptor sites on the myocardium. Expts. in which solns. of dibutyryl cyclic AMP [362-74-3], dibutyryl cyclic GMP [32266-35-6], or aminophylline were continuously perfused into the cockroach heart, failed to establish that cyclic nucleotides mediate neurotransmitter or hormone action on this tissue.

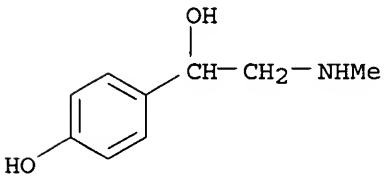
IT 104-14-3 16589-24-5
RL: BIOL (Biological study)
(heart response to, in cockroach)
RN 104-14-3 HCAPLUS
CN Benzenemethanol, α-(aminomethyl)-4-hydroxy- (9CI) (CA INDEX NAME)



RN 16589-24-5 HCAPLUS
CN Benzenemethanol, 4-hydroxy-α-[(methylamino)methyl]-, (2R,3R)-2,3-dihydroxybutanedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

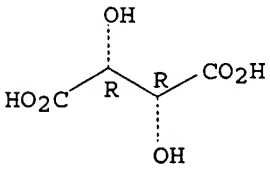
CRN 94-07-5
CMF C9 H13 N O2



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



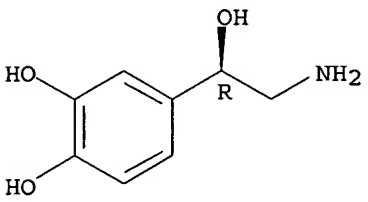
L38 ANSWER 87 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:93886 HCAPLUS
DOCUMENT NUMBER: 68:93886
TITLE: Site of action of pharmacologically active compounds on the heart of Peroplaneta americans
AUTHOR(S): Miller, Thomas Albert; Metcalf, Robert L.
CORPORATE SOURCE: Univ. of California, Riverside, CA, USA
SOURCE: Journal of Insect Physiology (1968), 14(3), 383-94
CODEN: JIPHAF; ISSN: 0022-1910
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Denervation of the American cockroach (P. americana) heart led to a simple myogenic heartbeat which was unresponsive to atropine, acetylcholine, and arecoline at concns. up to 10-3M, while the denervated heart responded by increasing its rate of rhythmic contraction when prefused with

5-hydroxytryptamine, d-tubocurarine, nicotine, tryptamine, dopamine, adrenaline, noradrenaline, and the carbamates m-isopropylphenyl N-methylcarbamate and 2-methyl-2-(methylthio)propionaldehyde O-(N-methylcarbamoyl)oxime (Temik). These responses support the idea that acetylcholine and atropine act on the cardiac nervous system, whereas the other compds. affect the myocardium. The neurogenic classification of the cockroach heart requires reexamn. A more appropriate classification is myogenic with extensive nervous control. 25 references.

IT 51-41-2, biological studies 51-43-4, biological studies
RL: BIOL (Biological study)
(heart of cockroach in response to)

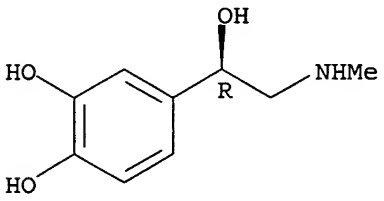
RN 51-41-2 HCAPLUS
CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 51-43-4 HCAPLUS
CN 1,2-Benzenediol, 4-[(1R)-1-hydroxy-2-(methylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L38 ANSWER 88 OF 88 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:6774 HCAPLUS
DOCUMENT NUMBER: 45:6774
ORIGINAL REFERENCE NO.: 45:1237c-d
TITLE: Local and systemic effects following application of dilute solutions of phenol in water and in camphor-liquid petrolatum on the skin of animals
AUTHOR(S): Deichmann, Wm. B.; Miller, T.; Roberts, J. B.
CORPORATE SOURCE: Albany Med. Coll., Albany, NY
SOURCE: Archives of Industrial Hygiene and Occupational Medicine (1950), 2, 454-61
CODEN: AIHOAX; ISSN: 0376-1096
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

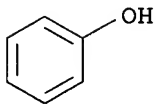
AB On application of 1.19 to 9.5% aqueous C6H5OH (I), 1.19 to 4.75% C6H5OH in aromatized liquid petrolatum (II), and 4.75 to 10.0% C6H5OH and 10.86% camphor in aromatized liquid petrolatum (III) to the tails of rats and to the skins of rabbits II was the most toxic, III the least toxic, with I

intermediate. The relatively low toxicity of III is due to the property of camphor to reduce the extent of the local action and absorption of C6H5OH.

IT 108-95-2, Phenol
(physiol. action of, after application in water and camphor-liquid petrolatum solns.)

RN 108-95-2 HCAPLUS

CN Phenol (8CI, 9CI) (CA INDEX NAME)



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